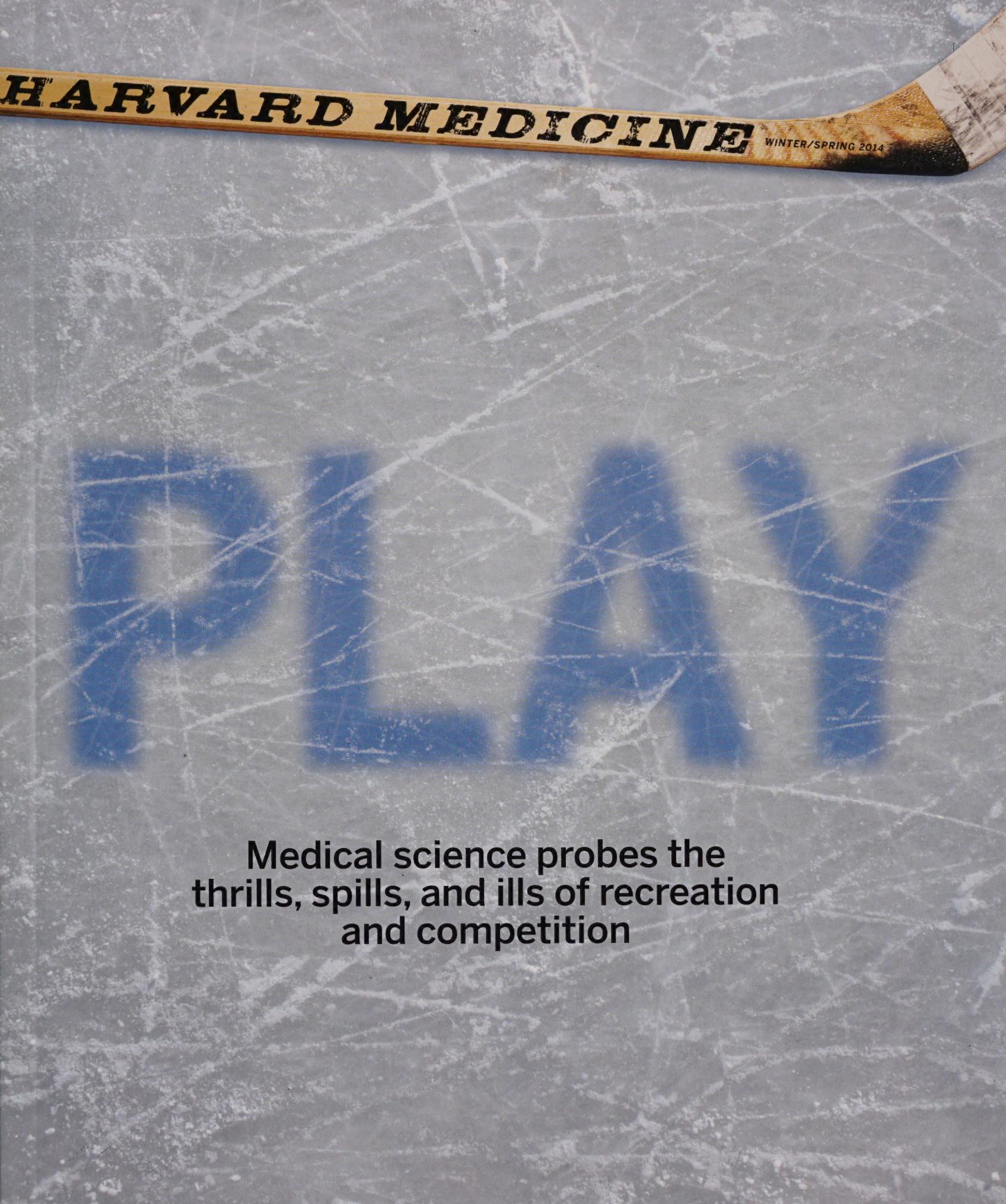


HARVARD MEDICINE

WINTER/SPRING 2014



**Medical science probes the
thrills, spills, and ills of recreation
and competition**

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CYCLE OF LIFE: Paul Dudley White (far right) promoted the merits of exercise and recreation well before such advice became fundamental to the prescription for a healthy lifestyle.





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From the Dean

THOUGHTS ON INNOVATION



ARE WE EVER TOO OLD TO PLAY?

At one time, perhaps not so long ago, the answer to that question would have been a quick and decisive "yes." Today, probably not. Not only have our society's attitudes shifted to accommodate the notion of recreation as a part of life, but for many of us, our passion for creative expression through physical activity is as much a part of our definition of self as is our work as physicians, researchers, and care providers.

Science, the stock we value, increasingly agrees with this particular weighting of variables. According to some researchers, adults work together better if they play together well, for play allows them to temper aggressions, relieve boredom, and forge solidarity. The

literature on children and play draws similar conclusions. But as one story in this issue points out, child's play also shapes a young brain, fostering skills that help with solving problems and regulating personal behavior.

Elsewhere in this issue of *Harvard Medicine*, we look at the toll that extreme exercise can take on us physiologically and mechanically—and how medical advances are helping to reduce those costs. We also explore the role of mentally preparing for competition, by considering not only what makes us compete but also what keeps us in the game even when we question our ability to perform. And we celebrate the role of those who cheer from the sidelines by spotlighting the work of three alumni who tend to the injuries of those who play professional sports.

We physicians have athletes great and small among our ranks: swimmers, runners, bicyclists, hikers, rowers, and, if the stereotype has an ounce of truth, more than our share of golfers. And increasingly, we preach what we practice by prescribing exercise for our patients.

As dean of this leading institution of medical education and research, play is rarely high on my to-do list. But I am reminded, even encouraged, to engage in it by someone I consider the perfect play co-conspirator: my granddaughter. With her, I know better than to say "I'm too old to play." But more importantly, I don't even consider it.

A handwritten signature of Jeffrey S. Flier.

Jeffrey S. Flier
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Letters to the Editor

CHART NOTES FROM OUR READERS

Small Talk

"A Way With Words," the article in the Autumn 2013 issue of *Harvard Medicine* that discusses how little children soak up language, was wonderful. There is a light-hearted side to this topic that readers may find amusing.

Several years ago a couple, both physicians, came to Harvard to enrich their medical experience. With them came their two children, ages two and four. Although their mother spent some time with me in the Neuro-Ophthalmology Division of Brigham and Women's Hospital, both parents were away from home several days each week. The children, therefore, spent time in day care.

After the family was here about a month, the children's mother told me this story.

The children had learned so much English so quickly that their parents had no idea what they, the kids, were saying to each other. And the children knew this. They could chatter away in the presence of Mom and Dad, knowing their parents hadn't a clue to what they were saying. Mom, in particular, was certain some boundaries were being stretched. Also, although the children understood all the Turkish that was being spoken at home, they refused to speak any Turkish at all, even when asked questions in that language.

I recently heard from the mother. Interestingly, she reports that their youngest no longer speaks English, but that the older child is tops in her class in the language.

DON C. BIENFANG '64

BOSTON, MASSACHUSETTS

Fathers and Sons

Thank you for publishing "Family," the article about successive generations attending HMS, which appeared in the Autumn 2013 issue of *Harvard Medicine*. It prompted me to revisit my own family's history at the School.

The Washburn family was first represented by George Hamlin Washburn (1860-1933), Class of 1886. Although born and reared in Constantinople, George elected to remain in Boston after graduation. He practiced obstetrics and gynecology, and also taught those subjects at both Harvard and

Take a Bough

I recall fondly my father's showing me the places at the medical school where his research was conducted. His career inspired me to go into pediatrics.

THOMAS C. WASHBURN '57
FERNANDINA BEACH, FLORIDA

Tufts Medical Schools. One highlight of his career was his mission to Turkey after World War I, where he served as the Near East Relief Committee's medical director for that nation.

His son, my father, Alfred Hamlin Washburn (1895-1972), graduated from HMS in 1921. He recalled driving his father on house calls in Boston and, in the summers, around Manchester-by-the-Sea. His career in pediatrics included practice and research, culminating in his appointment as director of the Child Research Council in Denver, where he oversaw a world-famous longitudinal growth project that studied human growth and development from before birth to adulthood. He also taught in the Pediatrics Department at the University of Colorado Medical School, where he conducted hematology research. I recall fondly my father's showing me the places at the medical school where his research was conducted. His career inspired me to go into pediatrics.

I graduated from HMS in 1957. My career has included practice, research, and teaching in the fields of pediatrics, internal medicine, and public health. I currently work one half day a week in a primary care clinic in our county's health department. Inspired and strongly supported by

our community, I started the Samaritan Clinic of Barnabas Center eight years ago. I continue to volunteer as a practitioner and as the medical director of this free clinic.

THOMAS C. WASHBURN '57
FERNANDINA BEACH, FLORIDA

Burning Issue

I read with interest the differing views on the use of medical marijuana presented in "Second Opinions" in the Autumn 2013 issue of *Harvard Medicine*. As I read the perspectives, I recalled that at one time, one often read that marijuana had 9 or 10 times the amount of tar found in tobacco. That led me to wonder whether long-term medical use of marijuana will lead to future cases of lung cancer, especially among those with heavy cigarette smoking habits.

RAYMOND E. JANKOWICH '55
STRATFORD, CONNECTICUT

Lester Grinspoon '55 and Kevin P. Hill reply:

Grinspoon: Since Donald Tashkin's landmark study on marijuana and lung cancer (reported in 2006 at the American Thoracic Society International Conference), no one now makes the claim that marijuana can cause lung cancer. That study, which involved 1,200 patients, came up with a slightly negative odds ratio, which has led Tashkin and others to ask whether smoking marijuana might not be somewhat protective of the lungs. In any event, even though cannabis has about four times as much tar as tobacco, it does not cause lung cancer.

Hill: The data are unclear on whether marijuana causes cancer: some studies point to a link, others don't. Marijuana definitely contains cancer-causing compounds. It seems likely that marijuana use increases risk for lung cancer, although not nearly so much as tobacco smoking does. More research, however, is needed.

Harvard Medicine welcomes letters to the editor. Please send letters by mail (Harvard Medicine, 107 Avenue Louis Pasteur, Suite 111, Boston, MA 02115); fax (617-432-0446); or email (harvardmedicine@hms.harvard.edu). Letters may be edited for length or clarity.



THE WORLD WITHIN

Two exhibits explore our fascination with our own anatomy

aFFIXED TO ARCHES OF METAL, the teeth gleam like a bony rainbow, sparkling gold and silver whenever light strikes a filling. At the base of the arches, the upper half of a set of handsome dentures perches on a bed of satin.

Created in 1887 by F. E. Sprague for his final project as a student at Harvard Dental School, the assemblage has considerable space dedicated to a beautifully calligraphed list of the dental procedures Sprague had mastered. And in a place of honor, Sprague set a plaque engraved with his name.

With tensions that run between fascination and repulsion and mortality and preservation, "Twenty-nine dental preparations under glass" exemplifies many of the themes that thread through *Body of Knowledge*, a special exhibit at the Collection of Historical Scientific Instruments in the Science Center at Harvard University. The exhibit, which showcases many objects from the collections of the Center for the History of Medicine at the Francis A. Countway Library of Medicine, runs concurrent with *The Nature of Every Member: an Anatomy of Dissection* at Harvard Medical School, a sister exhibit at the Countway Library.

Body of Knowledge explores the complex social and cultural contexts of the study of human anatomy in the Western world, with particular focus on the Renaissance, the nineteenth century, and modern periods. Anatomy is more than the scientific process of learning the structures of the body, argue the exhibit's curators; it is also entwined with history, religion, human curiosity, artistry, and the pursuit of a scientific understanding of life.

The team of curators—which includes David Jones '97, the A. Bernard Ackerman Professor of the Culture of Medicine; Scott Podolsky '97, director of the Center for the History of Medicine at the Countway; Dominic Hall, curator of the Countway's Warren Anatomical Museum; and Jack Eckert, public services librarian of the Center—challenge visitors to examine the varied roles of the anatomist as teacher, student, scientist, artist, showman, and, occasionally, criminal.

They pose ethical questions about the acquisition and treatment of cadavers for dissection before the advent of voluntary donor programs. At the same time, the curators invite visitors to consider the tumult of emotions medical students experience when they take gross anatomy.

Specimens showcase an array of vivid preservation techniques, from wax-injected blood vessels to a plastinated heart to cross-sectional slivers of a man's body immortalized in acrylic. Meticulous etchings and paper "flap" models, which offer glimpses into the body that are both scientific and voyeuristic, evolve into radiographic images and digital reconstructions.

A mobile app with the exhibit presents how today's horror movies and forensic TV shows echo yesterday's dissection amphitheaters. At once exquisite and morbid, educational and provocative, the exhibit shows how our fascination with our own bodies lives on.

—Stephanie Dutchen



David Roberts

OUTWARD BOUND

First HMS dean for external education named

DAVID ROBERTS '95, an HMS associate professor of medicine at Beth Israel Deaconess Medical Center, has been named the School's first dean for external education, a new leadership appointment at HMS. Roberts began serving in his new role in March and will complete the transition on July 1.

In his new role, Roberts will define and implement a strategic vision that will advance the School's educational goals worldwide and guide its initiative to produce a range

of educational programs that incorporate the latest technologies.

He will also work to build partnerships with academic and research constituents such as Quad-based departments, Harvard University, Harvard Catalyst, and HarvardX, the University's online education program. Roberts's areas of oversight will also include Harvard Health Publications and the Department of Continuing Medical Education.

"In this new position, David will be a core

member of my educational and broader leadership teams," says Jeffrey S. Flier, HMS dean. "He will work collaboratively with other HMS leaders and faculty to build infrastructure and programs, bringing our educational expertise to new and expanded categories of learners, both locally and around the globe."

Roberts currently serves at Beth Israel Deaconess as the associate director of the Carl J. Shapiro Institute for Education and Research, as director of the Office of Undergraduate Medical Education, and as director of the Academy of Medical Educators. He has led both the HMS preclinical courses and the Beth Israel Deaconess Principal Clinical Experience, and has received numerous teaching awards, including the respected HMS Faculty Prize for Excellence in Teaching.

Extended Family

Research on cancer biology and treatment receives new support

HARVARD MEDICAL SCHOOL has received \$90 million from Ludwig Cancer Research to establish a Ludwig Center to drive collaborative scientific inquiry and discovery. The center will be codirected by Joan Brugge, the Louise Foote Pfeiffer Professor of Cell Biology and chair of the HMS Department of Cell Biology, and George D. Demetri, an HMS professor of medicine and the Quick Family Chair of Medical Oncology at the Dana-Farber Cancer Institute.

"This gift provides a momentous opportunity for the entire HMS community to glean new insights into the basic biology of cancer as well as to accelerate the translation of basic research to improve patient outcomes," says Jeffrey S. Flier, HMS dean. The gift, made on behalf of the late Daniel K. Ludwig, founder of Ludwig Cancer Research, reflects a portion of a \$540 million gift divided equally among the six Ludwig Centers at U.S. academic institutions: HMS, Johns Hopkins, Memorial Sloan-Kettering Cancer Center, MIT, Stanford University, and the University of Chicago.

Adds Flier, "We recognize that Daniel and Virginia Ludwig were powerful advocates for excellence in cancer research. We are grateful to them for their generosity and their vision, and are committed to honoring their legacy by advancing the fight against cancer."

This is the second major commitment Harvard has received from Ludwig Cancer Research to support a Ludwig Center that draws on the expertise of faculty members across the HMS Quad as well as at its affiliated institutions, including those faculty who collaborate through 18 disease- and discipline-based research programs as part of the Dana-Farber/Harvard Cancer Center. These gifts will allow Harvard's cancer research community to build upon research activities, attract leading biomedical and cancer researchers, speed the pace of discovery, pursue findings through subsequent stages of research, and expand collaborations throughout the United States and internationally.

—David Cameron



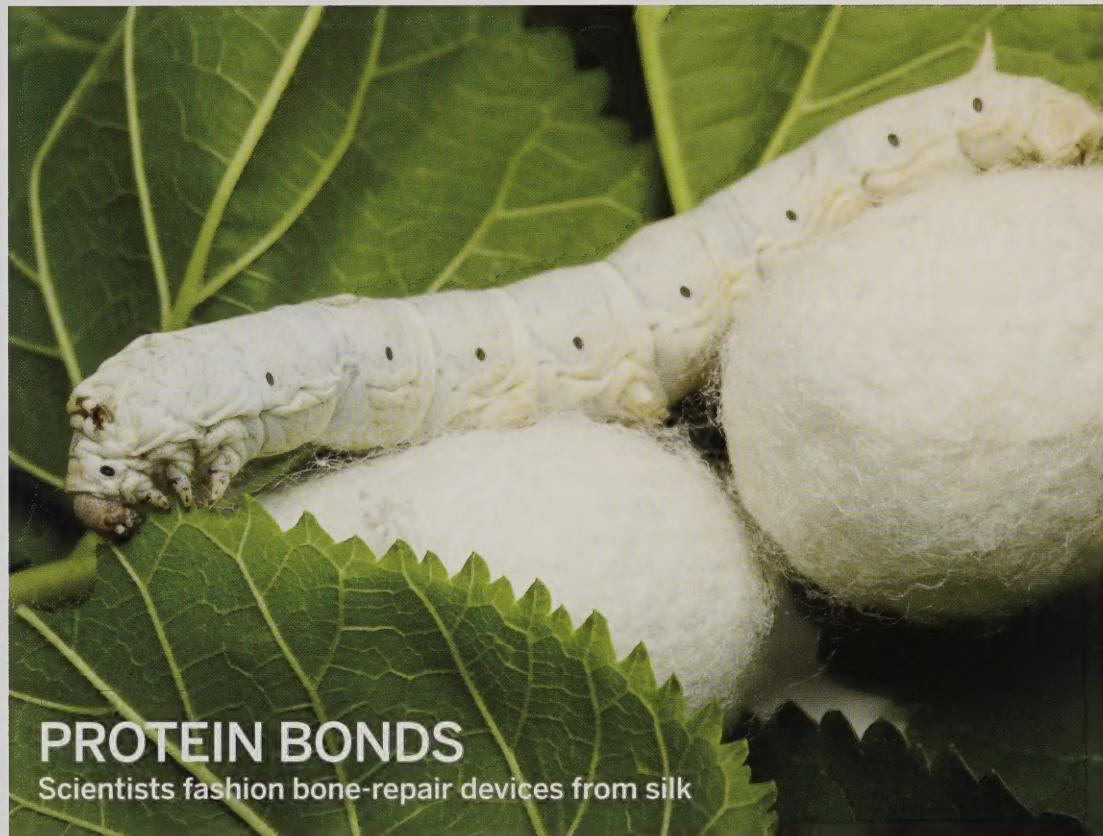
Four Words, One Community

Harvard Medical School has launched a community campaign called "I Am Harvard Medicine." Its goal: to celebrate the diversity and worldwide contributions of the people who make up HMS—students, alumni, faculty, staff, volunteers, and friends.

Join those who have shared their stories and photos online. Visit hms.harvard.edu/i-am-harvard-medicine and celebrate your contribution to the HMS community.

BENCHMARKS

DISCOVERY AT HARVARD MEDICAL SCHOOL



PROTEIN BONDS

Scientists fashion bone-repair devices from silk

WHEN SOMEONE SUFFERS A BROKEN BONE, treatment may call for a surgeon to insert screws and plates to help bond the broken sections and allow the fracture to heal. These so-called fixation devices are usually made of metal alloys.

Metal devices have disadvantages: their stiff, unyielding nature can stress underlying bone. They also pose an increased risk of infection. Resorbable fixation devices made of synthetic polymers avoid some of these problems but are difficult to implant and may trigger inflammatory reactions.

Recent research has identified a different substance, tested in an animal model and reported in the March 4 issue of *Nature Communications*, that may eliminate these disadvantages. That substance: silk.

A team of investigators from HMS, Beth Israel Deaconess Medical Center, and Tufts University School of Engineering has made surgical plates and screws from pure silk protein derived from silkworm cocoons. The devices are absorbed by the body over

time, eliminating the need for surgical removal, which can become necessary with metal devices.

"Silk materials are extremely robust," says co-senior author Samuel Lin, an HMS associate professor of surgery in the Division of Plastic and Reconstructive Surgery at Beth Israel Deaconess. "They maintain structural stability under very high temperatures, can withstand other extreme conditions, and can be easily sterilized."

According to the authors, silk can stabilize and deliver bioactive components, characteristics that would allow for fixation devices that deliver antibiotics to prevent infection, pharmaceuticals to enhance bone regrowth, and other therapeutics to support healing. In addition, unlike metal devices, silk ones do not show up on x-rays, making it easier for surgeons to use imaging to monitor the healing process.

Although the aim is to use silk-based screws to treat facial injuries, which occur at a rate of several hundred thousand each year, the devices could also be used for many types of bone fractures.

—Bonnie Prescott

Coast to Coast

Primary care physicians, whether rural or urban, are committed to quality improvement

FULL IMPLEMENTATION of the Patient Protection and Affordable Care Act (ACA) is expected to escalate the demand for visits to primary care practitioners. That demand may be strongly felt in rural primary care practices. Although studies have found that the quality of care delivered to patients in rural areas is as good or better than care provided in urban areas, the belief persists that top-quality primary care is available only in big cities.

A study published in the February 16 online issue of *The Journal of Rural Health* found that, regardless of location, physicians held similar attitudes on key measures of professionalism, including the value of participating in quality improvement.

"In terms of professional beliefs and behaviors, we found that rural and urban doctors are more alike than different," says study leader Eric Campbell, an HMS professor of medicine at Massachusetts General Hospital and director of research at the Mongan Institute for Health Policy at the hospital. "Despite our results and other evidence, the

perception still exists that rural primary care is not as good as that available in cities." Campbell and his colleagues decided to learn more about the factors driving that misperception, and the role it may play in the continuing shortage of rural physicians in this country.

The study was designed to determine whether there were differences between rural and urban primary care physicians in their professional beliefs and in their interest and participation in quality improvement activities.

For the study, a survey was sent to nearly 3,000 practicing physicians randomly selected from an American Medical Association database; slightly more than 1,800 responded. Of those who responded, 840 were family practitioners, internists, or general pediatricians. Based on zip code data, 127 respondents practiced in rural communities and 713 in urban areas.

There were no significant differences between rural and urban physicians' attitudes regarding participation in quality-improvement activities and the importance of open communication with patients, including reporting medical errors. Rural physicians were more likely to participate in error-reduction

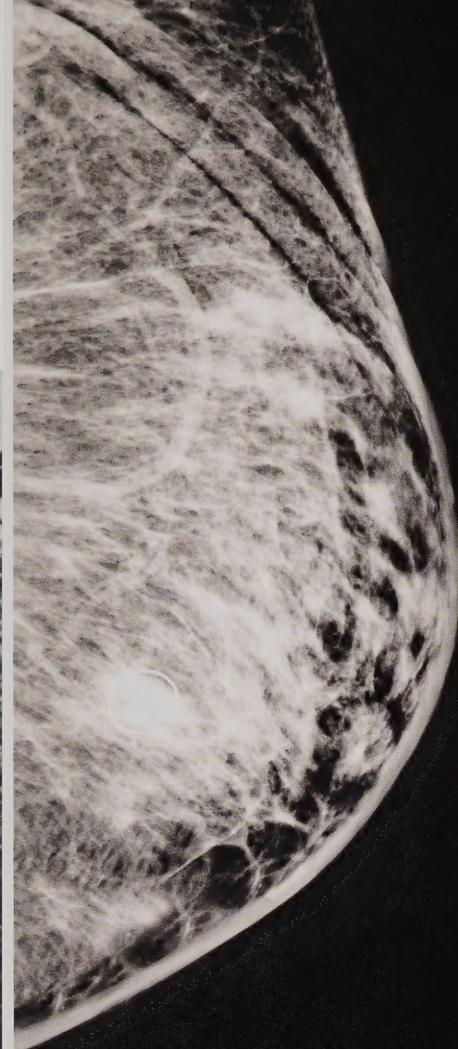
and other quality-improvement initiatives in their practices and hospitals and in reviews of other physicians' records, and they felt prepared to contribute to quality-improvement efforts. They also were more likely to agree that physicians should discuss the costs of care with their patients. In addition, rural physicians were more likely than their urban counterparts to have added Medicaid or uninsured patients to their practices during the preceding year.

In states that have not accepted the Medicaid expansion offered by the ACA, say the researchers, adding Medicaid or uninsured patients to a practice will place greater cost burdens on rural providers compared with those borne by urban doctors.

The researchers note that while smaller rural communities may have fewer training options, rural primary care physicians are more likely to have personal as well as professional relationships with their patients. This latter attribute, note the authors, may give the physicians a better sense of the environmental and lifestyle factors that affect their patients' health. That same attribute also could lead to challenges when professional responsibilities conflict with patients' expectations and perceptions.

—Sue McGreevey





Optical Conclusions

Benefit-risk concerns for mammography merit an individualized approach

A REVIEW of five decades' worth of international studies assessing the benefits and harms of mammography screening suggests that the benefits of screening are often overestimated, while harms are underestimated. The findings, say the researchers, indicate that physicians and patients need more guidance on how best to incorporate a patient's risk profiles and preferences into breast cancer screening decisions. The review by investigators in the Department of Health Care Policy at HMS and Brigham and Women's Hospital appeared in the April 2 issue of *JAMA*.

In 2009, the U.S. Preventive Services Task Force, employing an evidence-based analysis of the benefit-risk ratio of mammography, reversed its previous recommendation that women be screened every one to two years beginning at age 40, and instead recommended routine mammography every two years from age 50 on. That change remains controversial; in fact, recent evidence suggests that mammography use in the United States has not changed to reflect the updated recommendation.

"I tell my patients that the mammogram is not a perfect test," says Nancy Keating, an HMS associate professor of health care policy, associate professor of medicine at Brigham and Women's, and the study's co-author. "Some cancers will be missed, some people will die of breast cancer regardless of having had a mammogram, and a small number of people who might have died without screening will have their lives saved."

According to Keating, the chief harm associated with mammography is the risk of overdiagnosis: identifying cancers that never would have become problematic during a woman's lifetime, either because the cancer never grew or because the patient died first of another cause. Overdiagnosis can expose women to unnecessary surgery, chemotherapy, or radiotherapy. In addition, more than half of women who get annual screenings for a decade can expect to receive false positive reports. About 20 percent of false positives result in unnecessary biopsies.

—David Cameron



SECRETE SAUCE

Bioinspired adhesive can hold patches inside beating hearts

SCIENTISTS WHO LOOK TO NATURE for ways to improve the practice of medicine occasionally find nice surprises. When Pedro del Nido and Jeffrey Karp studied the secretions some creatures use to attach to surfaces wet or dry, they uncovered properties that inspired them to develop a nontoxic, waterproof, elastic, and biodegradable replacement for sutures, especially those now used to mend delicate heart tissue. Their report of this new surgical glue appeared in the January 8 issue of *Science Translational Medicine*.

"Current glues are either toxic, easily wash out in the presence of blood, or react immediately upon contact with water," says study co-author Pedro del Nido, the HMS William E. Ladd Professor of Child Surgery and chief of cardiac surgery at Boston Children's Hospital. "They also tend to lose their sticking power in the presence of blood or under dynamic conditions, such as in a beating heart."

In a preclinical study, del Nido, Karp, an HMS associate professor of medicine and co-director of the Center for Regenerative Therapeutics at Brigham and Women's Hospital, and colleagues developed an adhesive that can rapidly attach biodegradable patches directly on defects inside a beating heart. They found that the patches remained attached even at increased heart rate and blood pressure. In addition, because the glue's adhesive properties are activated rapidly by ultraviolet (UV) light, when placed, the patches can be sealed within five seconds of UV exposure.

"To our knowledge this is the first demonstration that an adhesive can bond to wet tissues and seal them without being affected by the presence of blood," says Karp. "We showed that the tissue glue can seal holes in high-pressure dynamic tissues, including blood vessels and the myocardium."

The researchers suggest the adhesive will help reduce the invasiveness of surgical procedures, shorten operating times, and improve heart surgery outcomes. The adhesive technology has been licensed for development and is expected to be commercially available within three years.



Escherichia coli are found in the human intestine.

Population Shift

Newly diagnosed Crohn's disease patients show rise in bad, drop in good, intestinal microbes

THE INTESTINAL MICROBIAL populations in patients newly diagnosed with Crohn's disease have been found to differ from those in people free of inflammatory bowel disease, says research from a multi-institutional study led by investigators from HMS, Massachusetts General Hospital, and the Broad Institute. Crohn's patients, according to their paper in the March 12 issue of *Cell Host and Microbe*, have increased levels of the harmful bacteria and reduced levels of the beneficial bacteria normally found in a healthy gastrointestinal tract.

Several studies have suggested that the excessive immune response that characterizes Crohn's may be linked to an imbalance in the normal microbial population, but the exact relationship has not been clear. The current study analyzes data from a tool designed to investigate microbial, genetic, and other factors. Participants were children newly diagnosed with Crohn's or other inflammatory bowel diseases as well as control participants with noninflammatory gastrointestinal conditions.

Advanced sequencing of the microbiome—the genome of the entire microbial population—in tissue samples taken from sites at the beginning and the end of the large intestine showed that, compared with samples from controls, Crohn's patients showed an abnormal increase in the proportion of inflammatory organisms and a drop in noninflammatory and beneficial species. The imbalance was even greater in patients with severe symptoms and in those whose tissue had markers of inflammatory activity.

None of the Crohn's patients had received treatment at the time of sampling. Antibiotics are often prescribed for symptoms suggestive of Crohn's before a diagnosis is made, and in participants who happened to be taking antibiotics at the time samples were taken, the microbial imbalance was even more pronounced, says senior author Ramnik Xavier, the HMS Kurt J. Isselbacher Professor of Medicine in the Field of Gastroenterology at Mass General and director of the MGH Center for the Study of Inflammatory Bowel Disease.

—Sue McGreevey

Many Hats

Gene regulator may play role in Alzheimer's and other dementias

WHY DO NEURODEGENERATIVE DISEASES such as Alzheimer's affect the elderly? Why do some people live to be over 100 with intact cognitive function while others develop dementia decades earlier? And why do others, despite having brains that exhibit pathologies associated with dementia, show few or no signs of cognitive decline?

According to recent research, an explanation for these longstanding mysteries may be found in a gene regulator called REST. Active during fetal brain development, REST switches back on later in life to protect aging neurons from various stresses, including the toxic effects of abnormal proteins. Now, work by a research team led by Bruce Yankner, an HMS professor of genetics, has shown that REST is destroyed in critical regions of the brains of people with Alzheimer's and mild cognitive impairment. The results were published online March 19 in *Nature*.

"Our work raises the possibility that the abnormal protein aggregates associated with Alzheimer's or other neurodegenerative diseases may not be sufficient to cause dementia; you may also need a failure of the brain's stress response system," says Yankner, who also codirects the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging at HMS.

The team found that REST is the most strongly activated transcriptional regulator—a switch that turns genes on or off—in the aging human brain. Until this time, REST's only known activity in the brain occurred prenatally, when it keeps key genes turned off until progenitor cells are ready to differentiate into functional, mature neurons. After birth, REST was known to stay active elsewhere in the body and perhaps to protect against several kinds of cancer and other diseases.

When the scientists looked at REST's role in aging neurons, they found it turns off genes that promote brain cell death and contribute to the amyloid plaques, neurofibrillary tangles, and other pathological features of Alzheimer's disease, and that it turns on genes that help neurons respond to stress.

The team found that high levels of REST also may act to thwart dementia, even in people whose brains, donated after death, show the characteristic pathology of the disease. The researchers also found evidence that REST may play a role in longevity. —Stephanie Dutchen



PRE-EXISTING CONDITIONS

Improved screening and early, enhanced interventions may help reduce soldier suicide rate

SOBERING DATA gathered in the largest study to date of mental health risk and resilience among U.S. Army personnel indicate that nearly 50 percent of soldiers who attempt suicide did so for the first time before they enlisted. In addition, the research, reported in three papers published online March 3 in *JAMA Psychiatry*, showed that more than 75 percent of soldiers who currently have mental health disorders experienced the onset of these disorders before entering the service, and that nearly 60 percent of soldiers who had ever considered suicide had such thoughts before enlistment. According to the researchers, the findings indicate that reducing the high suicide rate among soldiers may require improvements in the screening of applicants and enhanced interventions for new soldiers who have mental health disorders.

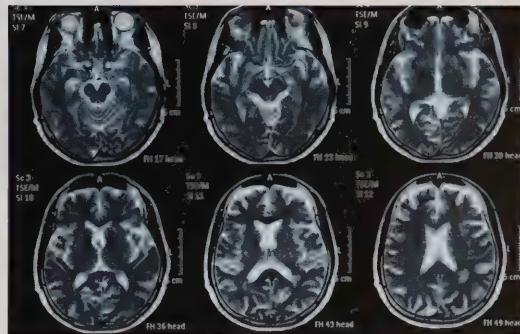
The data were drawn from responses to a survey called Army STARRS, Army Study to Assess Risk and Resilience in Servicemembers, which was developed through a partnership between the Army and the National Institute of Mental Health. The papers detail the different strategies the research teams used to evaluate suicide risk and protective factors among service members. One of the papers compared the prevalence of mental disorders among Army and civilian populations; its lead author is Ronald Kessler, the McNeil Family Professor of Health Care Policy at HMS.

"Some of the differences in disorder rates are truly remarkable," says Kessler. "The rate of major depression is five times as high among soldiers as civilians, intermittent explosive disorder six times as high, and PTSD nearly fifteen times as high."

The most common disorders captured in the survey were attention deficit hyperactivity disorder (ADHD) and intermittent explosive disorder (IED), which are recurrent and uncontrollable anger attacks, Kessler says.

The findings suggest that, before enlistment, the rate of anxiety disorders and depression, so-called internalized disorders, was not higher among soldiers than among civilians, but that the rate among soldiers rose after enlistment. By contrast, behavioral disorders such as ADHD, IED, and substance abuse were much more common among people who enlisted in the Army than among those who did not. Rates of these disorders rose even more following enlistment.

—Jake Miller



Arrested Development

Aspirin may inhibit growth of tumors responsible for hearing loss

RESEARCHERS FROM HMS, Massachusetts Eye and Ear, Massachusetts General Hospital, and MIT have shown that aspirin intake can inhibit the growth of vestibular schwannomas, intracranial tumors that typically cause tinnitus and hearing loss and are sometimes lethal.

Vestibular schwannomas, also known as acoustic neuromas, are the most common tumors found in the cerebellopontine angle, a fluid-filled space in the brain through which several cranial nerves pass. These schwannomas grow along the vestibulocochlear nerve, the cranial nerve responsible for transmitting auditory and balance information from the inner ear to the brain, and they develop from Schwann cells, which form the myelin that insulates nerves.

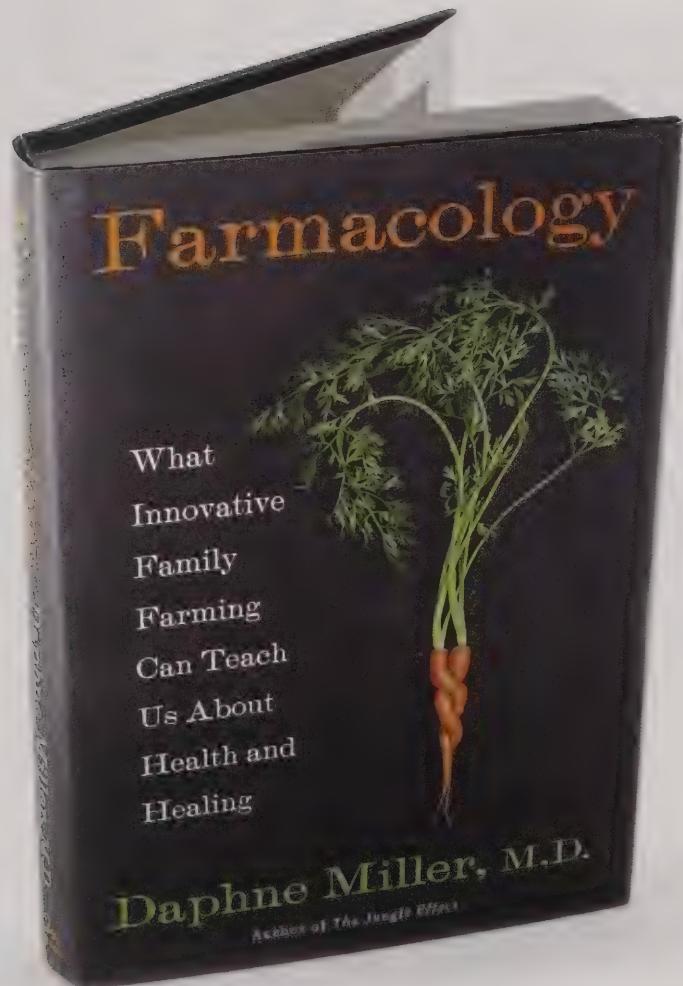
"Currently, there are no FDA-approved drug therapies to treat these tumors," says study leader Konstantina Stankovic '99, an HMS assistant professor of otology and laryngology at Mass Eye and Ear and a member of the faculty of the HMS Program in Speech and Hearing Bioscience and Technology. "Current options for the management of growing vestibular schwannomas include surgery or radiation therapy, each of which can have potentially serious complications." Surgical access to these tumors, for example, usually involves removing a section of the skull to expose the brain and provide a route to the tumor.

The findings, reported in the February issue of the journal *Otolaryngology and Neurotology*, were based on a retrospective study of 689 people who had been diagnosed with vestibular schwannoma at Mass Eye and Ear. Fifty percent of the patients had had their tumor progression monitored by serial MRI scans. The scientists gathered data on the rate of tumor growth as determined by changes to the largest tumor dimension measured in the MRIs, and correlated it with patients' use of aspirin. The researchers found that regardless of age or gender, the greater the use of aspirin, the smaller the rate of tumor growth.

—Mary Leach

BOOKMARKS

REVIEWING THE WRITTEN WORD



BACK TO THE LAND

Farmacology:
What Innovative Family Farming
Can Teach Us About Health and Healing
by Daphne Miller '93
(WILLIAM MORROW, 2013)

reviewed by Elissa Ely

SOIL AND THE HUMAN BODY have the same nitrogen-to-carbon ratio and pH range. The soil feeds us. We are the soil. A doctor could do worse than learn from a farmer. It's kismet.

Both farming and medicine, Daphne Miller '93 writes in her book *Farmacology: What Innovative Family Farming Can Teach Us About Health and Healing*, intervene "oh so judiciously—in the cycle of birth, growth, death, and decay." While Miller the farmer was interning her way through a variety of family farms, Miller the family practitioner was treating patients whose medical dilemmas seemed oddly similar to agricultural ones. The book is her plea for the creative integration of these two tending professions.

She first noticed similarities on a biodynamic farm in Washington State. Its owner had dutifully studied soil analyses and followed chemical recommendations. But land is not formulaic. When the owner of Jubilee Farm threw the lab printouts away, along with the pesticides, herbicides, and fertilizers guaranteed to boost the soil's health, a self-contained but vibrant eco-cycle developed. Cows roamed fields, fertilizing them through microbiota-rich manure; manure decomposed into topsoil; topsoil nourished crops; and crops fed cows and people, turning the wheel once more.

It becomes personal: you are what you eat when you eat where you are. Jubilee Farm's healthy results—and research into the evolving, almost magical, field of "gut ecology"—caused Miller to wonder whether, back in her clinic, a patient with "wilt" and "bloat" needed a microbial overhaul. She discontinued the restrictive diet and endless supplements, and prescribed entrance into an eco-cycle: local volunteer farm work, a community-supported agriculture share, and counterintuitive eating:

heavy on the outer parts of produce that had been "pest-nibbled, sun-exposed." Not one H2 blocker was in the treatment plan.

Miller roamed farther and met a cheerful, politically conservative rancher in Missouri who employed "the only free labor I had at my disposal, those billions of bacteria and other microbes in the soil." She met foraging, pasture-based chickens in Arkansas that caused her to investigate allostasis and stress reduction research in humans. She met a Sonoma vintner whose pest management system promoted beneficial insects. That meeting led her to look into a form of innovative cancer treatment called adaptive therapy—"seeing cancer more as a chronic pest and less as an invader." It's alternative living in a big way, whether you're the field, the cow, the cultivated insect, or the patient of a type of physician she calls "medical ecologists."

Miller had fun, writes exuberantly, and wants to infect us in the best way possible with the spirit of these places. I myself bought a slew of essential oils after she described the lovely skin of an aromatic herb farmer in Washington State who cured Miller's facial dermatitis. It's not their fault if they're still corked.

Integrative theories like these lie to the left and right of traditional medicine. But Miller argues that the time for medical reductionism is over: we have entered an era when the "focus of solving health ... problems by subdividing them into smaller and smaller parts has reached a point of diminishing returns." The ecological metaphor may be slow to seed and—forgive the ease of these images—quick to uproot, but it is one that Miller is planting, planting, planting.

Elissa Ely '87 is a psychiatrist at the Massachusetts Mental Health Center.

AUSCULTATION

LISTENING IN ON MEDICAL EDUCATION



Medical schools turn to the flipped classroom to help students learn

by Jasmine Rana

AS I SAT IN THE LECTURE HALL in the Tosteson Medical Education Center to take the last exam of my first year of medical school, I couldn't stop staring at the sea of faces. I whispered to the person next to me, "Are there really this many people in our class?"

When it comes to preclinical education, it's becoming clear that

there's no longer a one-size-fits-all method of teaching and learning. With a growing number of online resources, it's possible to never set foot in a lecture hall until exam day. As major curricular reforms are being discussed at HMS and other medical schools across the country, it's not unreasonable to consider whether there are alternatives or modifications to the traditional lecture format that may better help students integrate the high volume of information presented in the preclinical years.

I was reflecting on this situation last spring when an e-mail message caught my eye. Khan Academy, an online nonprofit educational organization, was announcing that, together with the Robert Wood Johnson Foundation and the Association of American Medical Colleges, it was sponsoring a competition to seek individuals who could create free online educational videos for students preparing for the 2015 MCAT. As someone who is passionate about teaching, I was immediately sold. But its appeal was greater than that: This opportunity struck me as a way to better learn how technology outside of the classroom might be used to enhance medical education, including my own.

I had glimpsed the potential of educational videos during my first year at HMS. Richard Schwartzstein '79, the Ellen and Melvin Gordon Professor of Medical Education and course director of my class's physiology block, had recorded Khan Academy-style "chalk-talk" videos, 20 to 30 minutes in length, on several fundamental concepts in pulmonary physiology. In an inversion of the traditional lecture format—an approach he described

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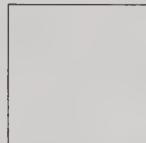


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as a flipped classroom when he introduced it to us during our first day of class—these videos were assigned as homework. We were to use them to prepare for the critical-thinking sessions of clinical vignettes in lecture. I considered this format to be better than the traditional lecture format: A well-structured 20-minute educational video can often transmit information far more effectively than 60 text-heavy PowerPoint slides.

I do not think we medical students should be spoon-fed our education. Learning how to adapt to different learning styles and to take ownership of how we incorporate new information are valuable lifelong skills. Grappling with uncertainty can be a good thing. Grappling with information overload, however, is not. Solving the latter is, I think, where good teaching outside the classroom comes in.

Technology has given us the tools to become self-learners. But how do we make individualized learning more productive? I was about to find out: I had been accepted into the Khan Academy training session.

Equipped with my laptop, a microphone attachment, and a writing tablet, I flew to San Francisco for the weeklong session. I and the 13 other participants from across the country—the majority of whom, not surprisingly, were medical students—met Rishi Desai, Khan Academy's medical fellow. Desai has made countless medical and health care educational videos for Khan Academy on topics ranging from the alveolar gas equation to atherosclerosis. I had, in fact, discovered many of his videos on YouTube and had benefited from their content during my first-year courses.



Technology has given us the tools to become self-learners. But how do we make individualized learning more productive?

Our training week focused on making—and critiquing—videos. Conversations about preparing content for the MCAT flowed into discussions about our own educational experiences. Throughout the week, one question kept coming up: could this model for creating a structured online classroom be the next step in medical education?

One night over dinner, a participant who had just finished his first year in medical school told us how he had made Khan Academy-style videos for his classmates. He had realized that the Khan Academy approach

would suit a lot of topics in medical education, so he bought a writing tablet for his computer and started fooling around with it.

"I made videos on whatever we were learning at the moment and shared them with my classmates," he explained. "People liked them, as they like any well-digested presentation of what we need to know. I think they liked the clarity, because a lot of the lectures we receive are difficult to follow."

Many of us around the table shared similar sentiments about our preclinical education. As we discovered, however, making effective educational videos isn't easy. In a classroom, facial expressions and gestures add rich layers of engagement. But in a chalk-talk video, there is only a voice in the background and a pen marking a virtual blackboard. Sound quality, engaging color choices, pacing, and clarity are all important considerations in video production. Despite the challenges, it was powerful to discover that making an educational video is not above anyone's head—at a minimum, all it requires is a laptop, a writing tablet, and practice.

In retrospect, the training session gave me a greater understanding of the positive role that technology can have in the evolving student-teacher relationship. By producing clear, focused, bite-sized chalk talks that begin with the big picture and then slowly bring in the details, Khan Academy's videos allow individuals to tackle and master concepts at their own pace.

The chalk talk model may be especially useful for medical students, considering the information overload challenge we face. Students in my class at HMS, for example, come from diverse academic backgrounds—

business, cell biology, economics, math, political science, and public health, to name a few—and, consequently, have vastly different aptitudes for the subjects required in medical school. Given the quantity of knowledge medical students must absorb and understand, it is not unreasonable for them to want to build individualized learning plans that accommodate different baseline levels of understanding the material.

Pursuing a path of self-learning, however, has its pitfalls. Midway through several courses this past year, I found myself surrounded with more textbooks and online resources than I had time to use. Instead of complaining about a lack of resources, I most often found myself complaining of too many. Sorting through all the noise was the biggest hurdle. A guiding framework that organizes all the information is often lacking or difficult to glean from material presented in a large lecture hall. Bite-sized educational videos may be just the sort of engaging framework for content that students could use outside the classroom. I do hope, however, that such videos would enhance, rather than replace, peer-to-peer and peer-to-educator interactions inside the classroom. ■

Jasmine Rana '16, a second-year student at Harvard Medical School, participated in the Khan Academy video development workshop during the summer of 2013.

The opinions presented are those of the contributor and do not necessarily reflect those of the President and Fellows of Harvard College or the publishers of Harvard Medicine magazine.





Free play shapes a child's brain—and bestows a lifetime of benefits
by Jake Miller

CHILDREN'S GAMES, PIETER BRUEGEL THE ELDER, 1560, KUNSTHISTORISCHES MUSEUM, VIENNA

FLIGHTS OF FANCY

A five-year-old in a pink and purple striped sweatshirt bares her teeth, growls, then plunges into a knot of snarling children. ■ In the scrum, a dozen kids ranging in age from almost three to just over eight are roaring and roughhousing their way through a game they have just improvised: lion-cheetah wrestling. The bigger children snarl as they grapple with one another while the smaller ones spar gently, cavorting on all fours on the edge of the tumble. ■ This chaotic, jubilant scene reflects what researchers in neurology, psychology, evolutionary biology, educational theory, and wildlife biology consider to be a powerful technique for building brains: child-driven free play.

P

lay fosters empathy and makes possible complex social groups, according to researchers who study brain development and behavior. Early childhood educators, as well as managers in diverse fields who need to hire skilled problem solvers, find that a strong foundation of childhood play is at the core of imagination and innovation. Play may even serve as a short-term boost for problem-solving skills: cognitive scientists have found that young children who approach problems within the context of play are able to solve logic problems often considered beyond their cognitive abilities.

Play is more about process than content. At its best, play is self-directed and guided by fluid rules agreed to by all participants. But whether it is raucous or quiet, physical or mental, social or solitary, the act of playing seems to open the brain to possibilities. It is perhaps one of the best tools we have for developing our brains in ways that can help us learn how to survive in an unpredictable world.

Wild Life

Researchers have found that in nature, species that exhibit playful behavior tend to be smarter and more adaptable than less-playful or nonplayful species. Long-term studies designed to assess the evolutionary cost or benefit of play among grizzly bears on Alaska's Admiralty Island measured the playfulness of young bears, then followed them into adulthood to see how they fared. Members of the more playful groups showed a greater likelihood of surviving into adulthood and, consequently, of reproducing, than those that were less playful.

Laboratory studies also have shown that young mammals deprived of opportunities to play or given only rote learning tasks have brains that are physically less developed



than those of their frolicking peers. In addition, research has found that play-deprived primates are less able to deal with stress, which can result in fearful behavior in unfamiliar circumstances and overly aggressive social interactions.

We may be seeing evidence of these same effects in human children. Since the mid-twentieth century, say some experts, there has been a decline in the time allowed children for free play. During this same period, psychiatrists have tracked in children a rise in narcissism, depression, anxiety, and feelings of helplessness. The parallel between the results of animal experiments and these demographic trends hints at a causal relationship, researchers say, adding that the move from free-ranging childhoods to more structured school environments, less time for recess or play, and a greater number of organized extracurricular activities for even the very young may also be stunting the rising generation's ability to think creatively and solve problems.

Old School

Insight into how children's lives have changed throughout the millennia—moving from more free time to more structured time—can begin to be gleaned from anthropological reports of

extant pre-agricultural cultures. In hunter-gatherer societies, youngsters spent much of their youth making up stories, songs, and games; mirroring adult activities; and learning how they and other living things meshed with the environment.

"Unstructured play was, and is, how children learn how to learn," says Susan Linn, an HMS instructor in psychiatry and a research associate at Boston Children's Hospital. "They learn to experiment, and they learn that they have the power to make changes in their world."

Linn, who pioneered play-based therapies to help children cope with hospitalizations and other traumatic events, studies the effect that diminishing opportunities for child-driven play can have on developing brains.

"Child-driven, hands-on play is the foundation of creativity, constructive problem solving, and the capacity to self-regulate," Linn says. "It's the way that children wrestle with life to make it meaningful. It is, in itself, a survival skill."

A recent study compared the cognitive outcomes of children in conventional preschool classrooms with those of children in Montessori classrooms. The researchers found that children in Montessori classrooms, which feature mixed-age



FAMILY FRIEZE: Opportunities for children to engage in free, unstructured play have diminished over the generations. Today, children's playtimes often include some level of adult oversight and participation.

populations and emphasize hands-on learning and play, showed greater gains than their peers in conventional programs in reading, math, and vocabulary, as well as in social competence and self-regulation. The latter is behavior driven by the brain's prefrontal cortex, the seat of high-level cognitive processing.

And it's not all or nothing. Researchers have found unstructured play to be helpful, even in small doses. In studies of kindergartners and elementary school students in schools that rely on structured learning, recess has been shown to improve children's ability to pay attention and assimilate new knowledge and skills.

Shapeshifting

Learning changes the brain. As we learn, new synapses form, adding connections in response to stimuli from the environment.

This capacity for change, known as plasticity, is amplified by just the sorts of experiences that play allows. Free play provides an environment rich in stimuli that can spark the formation of new neural connections. A child's imagination can also trigger new connections that biologically tie together distinct areas of the brain and cognitively link seemingly disparate experiences.

You can develop your brain just like you develop your muscles through exercise, says neuroscientist Majid Fotuhi '97. Doing exercises you don't like—push-ups and pull-ups in the gym, for example—will provide some of the necessary stimulation to build your muscles, but the anxiety caused by a demanding workout or by the pressure to get fit releases stress chemicals. The stress associated with cognitive workouts—like cramming for high-stakes tests—can be especially counterproductive.

"In structured learning, you're stimulating one part of the brain, but if it's too stressful, it comes at the cost of increasing cortisol production, which inhibits learning and memory. It's basically toxic to the rest of the brain," Fotuhi says.

Fotuhi, founder and chief medical officer of the Maryland-based NeurExpand Brain

Center, takes an integrated approach to brain health, emphasizing that cardiovascular fitness and proper diet are also crucial to neurological and cognitive well-being.

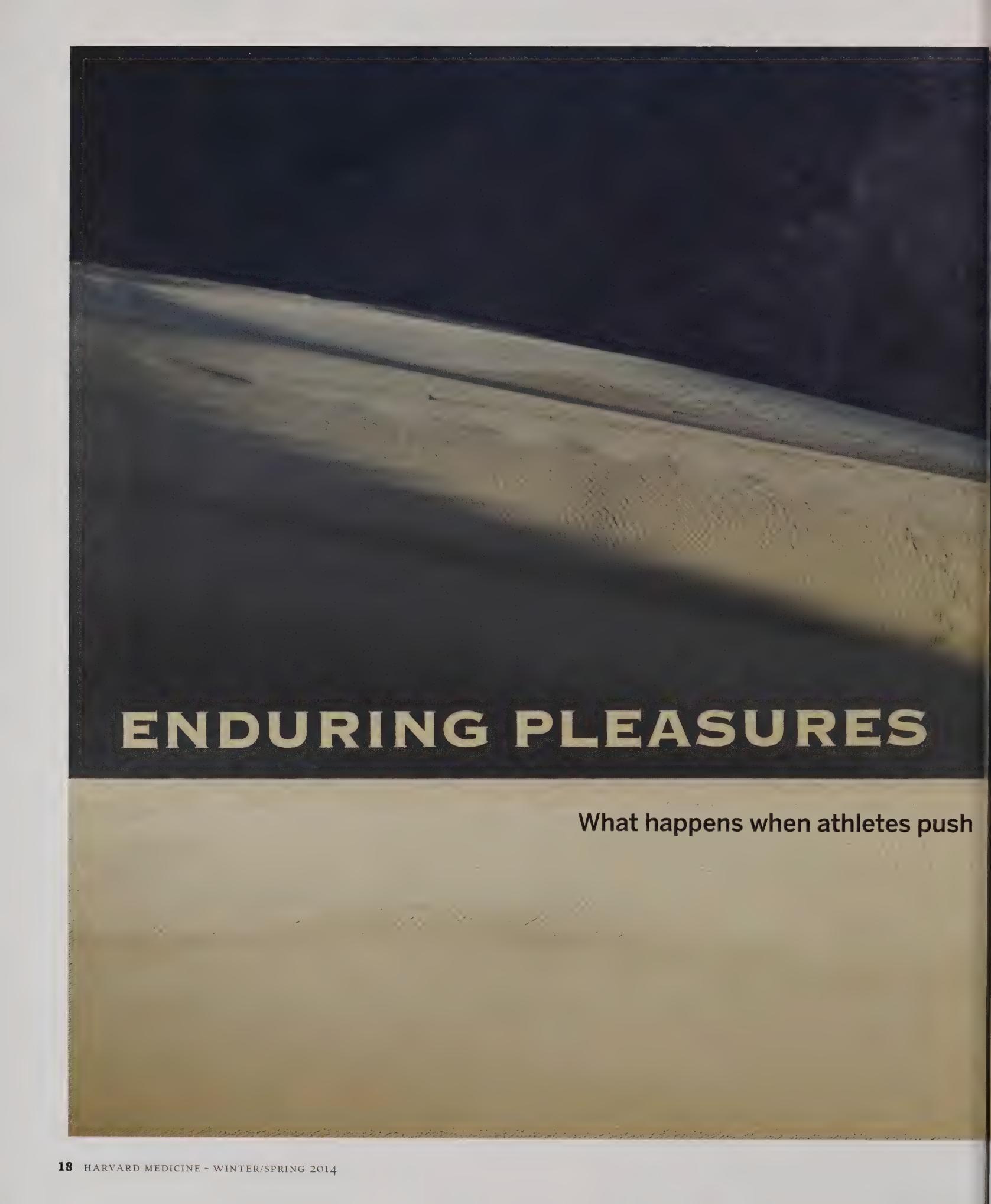
For children, his prescription for a brain-healthy lifestyle includes physical exercise and a balance of structured learning and free play. In his personal life, he's had the opportunity to see how unstructured play allows his seven- and eight-year-old daughters to explore their talents and interests.

One daughter loves building structures with Lego blocks, solving puzzles, and doing mathematical problems. When Fotuhi comes home, she asks about the more interesting cases he had that day. His other daughter loves art, and spends her free time drawing and painting, listening to music, and designing creative costumes for her dolls.

"They're going to be happier, more successful, and have better brain development if they do what they love than if we try to force them to learn what we want them to learn," he says.

It is not hard to imagine a pack of lions and cheetahs, some clad in pink and purple stripes, roaring in agreement. ■

Jake Miller is a science writer in the HMS Office of Communications and External Relations.



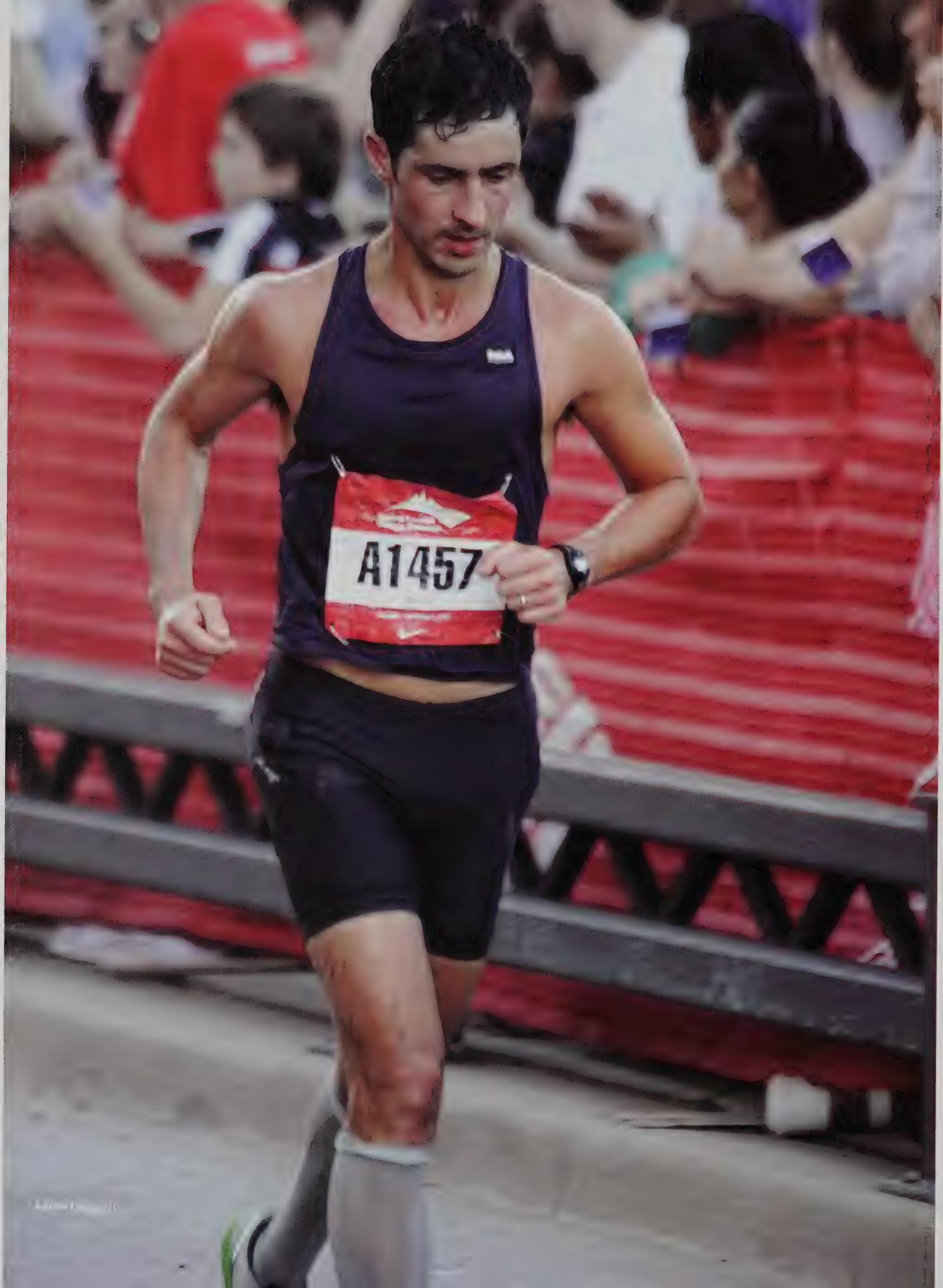
ENDURING PLEASURES

What happens when athletes push



themselves to their physical limits? *by Elizabeth Cooney*

Aaron Baggish passes a grapefruit-sized wooden ball from hand to hand. Hewn from pine, the sphere wears hundreds of almond-shaped gouges on its honey-colored surface. ■ This type of *bola* is used by the Tarahumara people—"those with nimble feet." They kick it over rocky trails in the rugged Copper Canyon region of northern Mexico as part of a centuries-old festival called Raráipari. They run as teams from early morning through the night and into the next morning, all the while moving the ball forward with their feet. It is a ritual we would call an endurance contest. They call it a game of life.



They don't run very fast; they just run for long periods," Baggish says. "The turning of the ball represents the turning of the world, and moving the ball as a team symbolizes interacting with a turning world in a healthy way."

Baggish, an HMS assistant professor of medicine and a cardiologist at Massachusetts General Hospital, visited the Tarahumara people with his running partner Daniel Lieberman, the Edwin M. Lerner II Professor of Biological Sciences at Harvard, who is an evolutionary biologist and an evangelist of barefoot running. Baggish brought more than the *bola* back to Boston. The day before the Raráipari, he secured ultrasound images of the hearts of the best runners so he could compare them to like scans of indigenous people who had moved into towns and, unlike the Tarahumara, left their running habits behind.

Judging by those scans, Baggish says, the hearts of the runners were large, just like the hearts of Olympians and other supremely gifted athletes who are devoted to regimens that help them deliver first-rate performances. Yet when Baggish asked the Tarahumara runners about training, he learned that the concept was foreign to them. So was the concept of exercise. They run to get someplace faster than if they were to walk. A couple of times a year, they run day and night in long competitions that are celebrations meant to set the world in balance.

Outside the Copper Canyon, endurance events may seem designed to pluck at extremes rather than embrace balance. Ambulances trailed the first band of 15 Boston marathoners in 1897; there was a fear that the runners would not survive their run through the winding roads of Eastern Massachusetts. More than a hundred years

later, the competitive challenges taken on by endurance athletes still inspire a healthy dose of skepticism. The sports these athletes participate in include not only running but also rowing, cross-country skiing, cycling, and swimming; in short, any continuous physical activity guaranteed to demand maximal oxygen intake by the athlete.

Physicians and scientists like Baggish are building a body of research to illuminate what happens when we push the limits of our physical selves. He studies, for example, young athletes on the cusp of rigorous training that may sculpt their hearts for a lifetime. Baggish also screens young people to determine whether they carry a congenital, often undetected, flaw that could, in the throes of intense athletic effort, set them on a path toward sudden cardiac arrest. And he helps older athletes with high blood pressure or elevated cholesterol levels adjust their medications—and their expectations—so they can stay active in the sports they passionately pursue.

"There's this myth that everything about exercise is good for you," Baggish says. "You're not going to find a cardiologist anywhere who advocates for exercise more than I do. But on the high ends of both strength and endurance exercise, there may be a price to pay down the line."

Alternative Energy

How much is too much of a good thing? According to many researchers, we really don't know. Exercise physiology is a young discipline, Howard Knuttgen reminds us, getting its start in North America in the 1950s, perhaps half a century behind its advent in Europe. Knuttgen, an HMS research associate in physical medicine and rehabilitation at Spaulding Rehabilitation

Hospital, points out that enshrining exercise as part of a healthy lifestyle is a relatively recent development.

"In the late 1940s, when I was in college," he says, "there was no evidence that physical activity had any effect on longevity. There were many physicians who pooh-poohed the need for exercise."

A researcher trained in exercise and muscle physiology in both Denmark and the United States, Knuttgen has served for more than two decades as the coordinator of scientific publications for the Medical Commission of the International Olympic Committee. Throughout those years, he says, instrumentation that can measure biochemical and physiological changes improved significantly, allowing advances in our understanding of how the human body performs athletic feats.

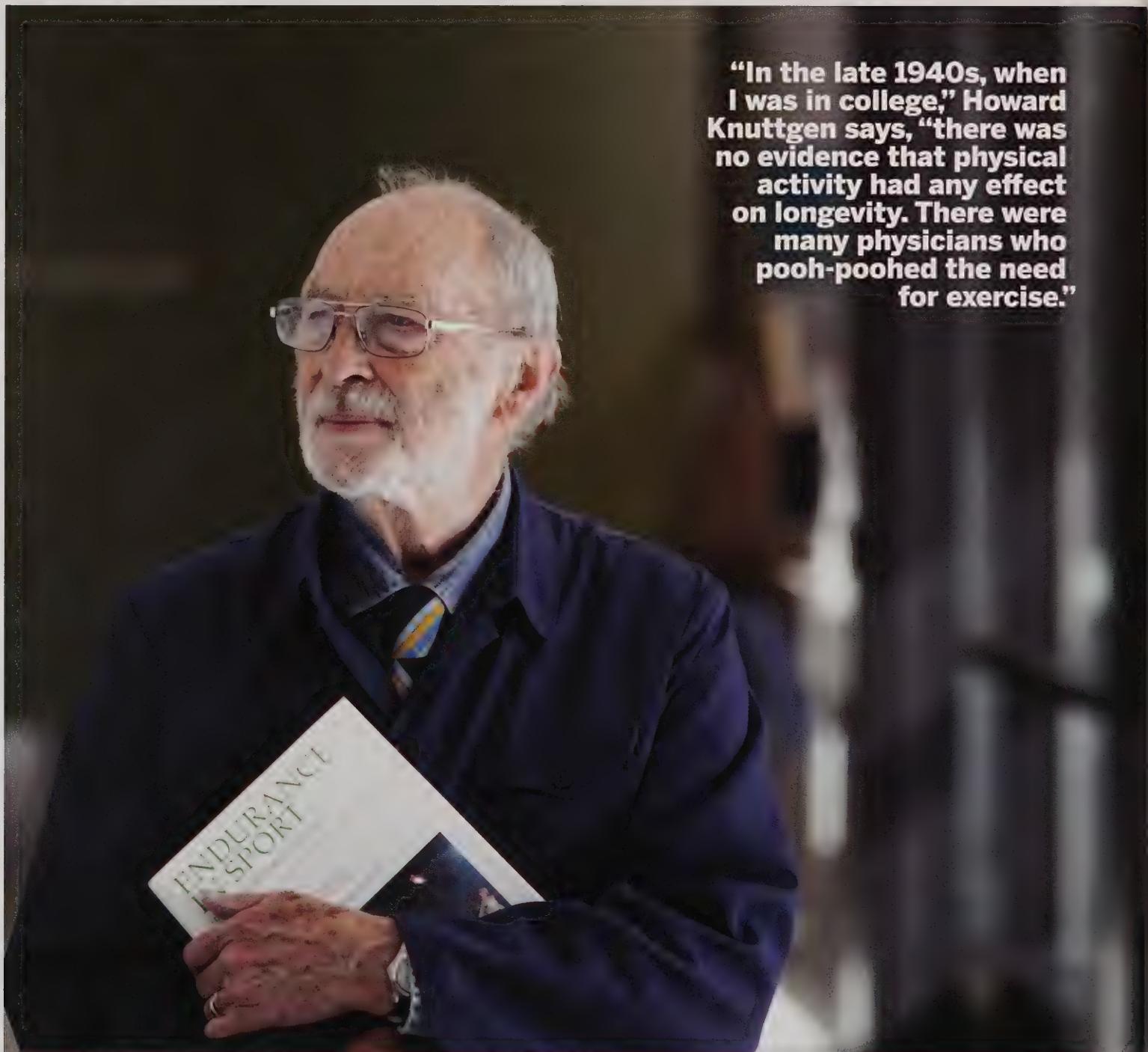
Although strength and endurance in sports are often considered synonymous, from a biophysical perspective they are poles apart, starting with the fuel that powers a single movement or thousands of repeated movements. Imagine a weightlifter, for example, marshaling her muscles for a hoist of the heaviest set of weights in the gym. The exertion requires her muscle cells to tap the high energy packaged in the compound adenosine triphosphate, better known as ATP, for the fuel needed for an intense burst of power. Such an energy expenditure allows one, perhaps two, such movements before exhaustion.

Contrast her effort to that of a long-distance runner, who may hammer out twenty thousand steps to complete a marathon. His muscle cells require a measured output of power: the aerobic metabolism of carbohydrates and fats. Drawing upon this resource supplies the muscles with a flow of energy that's less intense but longer lasting. Exhaustion occurs, but after a prolonged period of exertion.

Sports conditioning increases the body's number of capillaries to help ferry oxygen to muscles. Aerobic conditioning also improves the metabolic capacities of some muscle cells to use oxygen to convert carbohydrates or fats into energy. Distance athletes further amp up their maximum oxygen capacity by performing high-intensity speed workouts on days opposite their longer, slower training sessions.

Feel the Burn

Endurance sports training sets up a cycle of tissue injury and repair that helps improve



"In the late 1940s, when I was in college," Howard Knuttgen says, "there was no evidence that physical activity had any effect on longevity. There were many physicians who pooh-poohed the need for exercise."

conditioning and performance over time. Exercise is a form of stress recognized by all of the body's systems. Some degree of very mild injury comes with that stress, followed by beneficial repair. Over time, consistently injuring and repairing tissues develops a strengthened response.

Arthur Siegel '67, an HMS associate professor of medicine and chief of internal

medicine at McLean Hospital, worries about the inflammation that muscle injury can ignite during races that are typically longer and more intensive than any training run. He has grave concerns about the health of some distance runners when they are two-thirds of the way through a marathon. For Boston runners, that point is known as Heartbreak Hill, the dreaded stretch in Newton where competitors can fade.

By the time they hit that two-thirds mark, runners have spent their carbohydrate stores and are running on fumes. Among runners, it's known as hitting the wall; for Siegel it portends a different kind of crash: heart attack. Blood samples taken from healthy marathon runners after they crossed the finish line gave values that showed anything but health: The blood samples revealed



Heart, Shaped

In 2006, Baggish launched the Harvard Athlete Initiative to gather research on two groups of athletes: football players and rowers. Football players are strength athletes who use explosive bursts of power to charge down the field, tackle an opponent, or ready themselves for a collision with a rival bent on doing the same. Rowers are endurance athletes, pulling their oars and pushing their legs in a rhythm that sends slender boats slicing through the water.

The athletes look different—muscular linebackers can be as large as bodybuilders, while rowers tend to be as lean as their shells. Their hearts look markedly different, too. In endurance athletes, imaging reveals thin, supple walls surrounding the chambers of the heart. The chambers themselves enlarge over time so they can pump the amount of blood needed to meet the muscles' demand for oxygen; the heart's rate doesn't increase, but the volume of blood it can circulate does.

signs of inflammation similar to those found in patients with heart disease. Among the runners, however, the signs of inflammation subsided within a day.

That transient inflammation, Siegel says, is the result of stress that occurs when muscle injury starts an inflammatory cascade that also thickens the blood, which may then clump, blocking arteries and starving the heart of oxygen.

For strength athletes, imaging shows that the walls of their hearts' chambers are thick. One thing that concerns Baggish is the stiffness of those thick walls, which resembles that found in the heart chambers of middle-aged men with high blood pressure.

For endurance athletes such as runners, the overall incidence of cardiac arrest during or directly after a marathon is very low, according to an analysis of a decade's worth of data that Baggish published in 2012 in the *New England Journal of Medicine*. Distance matters, however, as does gender. The incidence was significantly higher among participants in marathons compared with those running half marathons and among men compared with women.

In the Long Run

"When you run a marathon, you are crossing the Rubicon," Siegel says. "You're going into a state of muscle injury."

His solution? Aspirin. He recommends that runners, especially men over age 45, take a small dose just before a race. Siegel is the first to say, however, that among physicians his is a minority opinion. But the medical director of the 2014 Rio de Janeiro Marathon includes a recommendation that male athletes over 40 take a low-dose aspirin if authorized by their physician.

Baggish and Siegel both urge more research on athletes. Baggish is accruing evidence through the work of the Harvard Athlete Initiative, believing that an ideal time to study the lasting effects of exercise is not after Olympic athletes climb the podium, but before freshmen begin their college sports careers, while their bodies are still being molded. In addition, he hopes to describe the physiological effects of exercise in the nonathlete. Such insight would be useful; in the clinic, says Baggish, physicians still don't know how much movement to prescribe.

Baggish will be again turning to the Tarahumara runners to compare their long, steady, slow running to the competitive athlete's mix of high speed and hard distance.

"I think we're going to learn that duration and intensity provide two very different signals," he says.

Finding a balance between these signals may answer at last how far and how hard we should push ourselves. ■

Elizabeth Cooney is a science writer in the HMS Office of Communications and External Relations.

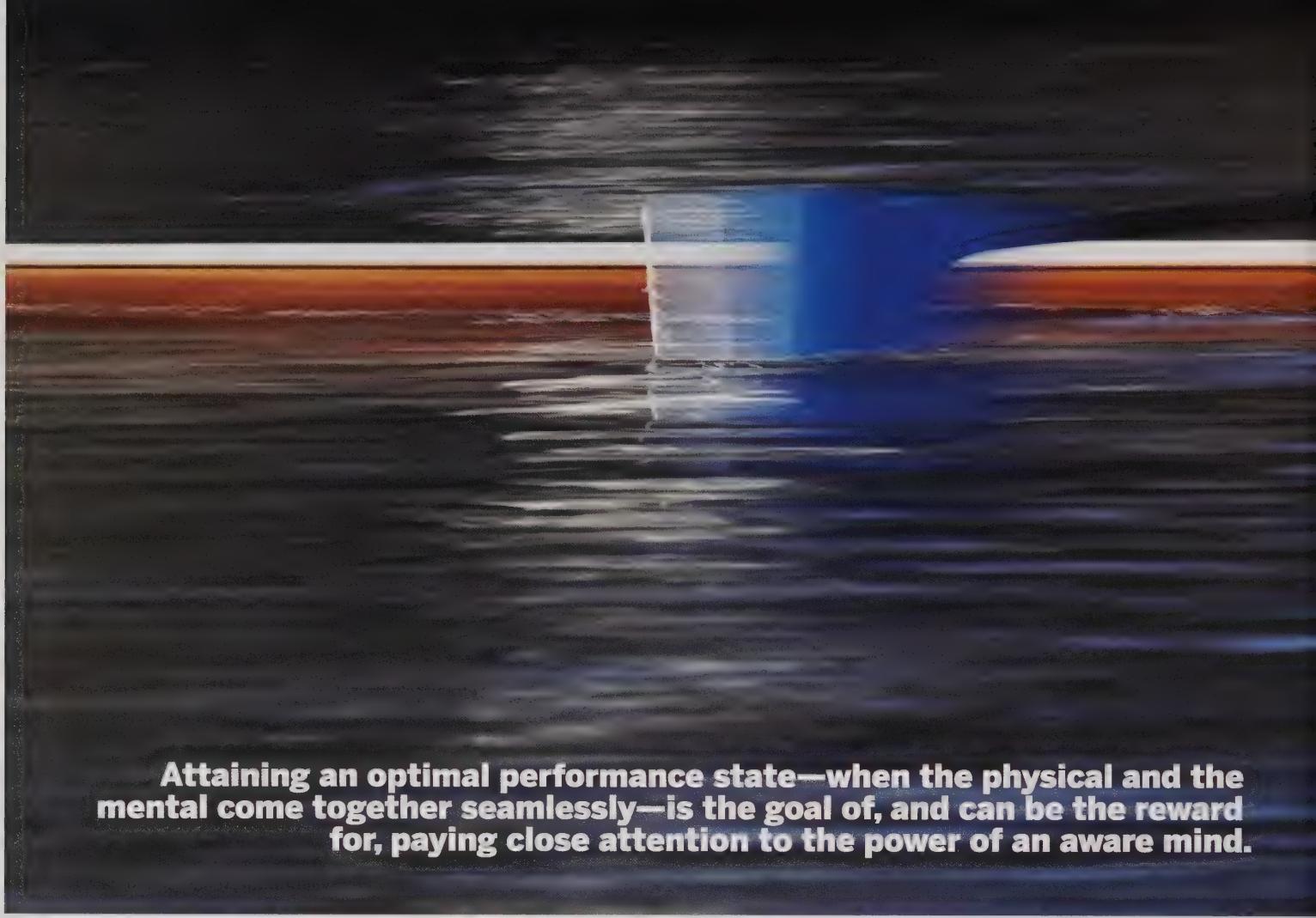


Competitive Edge



Practice might get you to the Olympics, but mental preparation may be what puts you on the podium
by Susan Karcz

Yogi Berra, the eminently quotable former New York Yankees player and manager, is credited with saying that “90 percent of the game is half mental.” Research may bear him out: How elite athletes handle the pressures of competition is determined by years of practice. Training the body without also preparing the mind, however, may undermine the fruits of physical effort when an athlete is faced with the rigors of competition. ■ During a big race or a deciding game, many factors are beyond human control: weather, equipment integrity, and unexpectedly strong opponents. Although an athlete may not be able to stop the rain, she can control her own training and preparation.



Attaining an optimal performance state—when the physical and the mental come together seamlessly—is the goal of, and can be the reward for, paying close attention to the power of an aware mind.

Notes or Barres

Saiya Remmler '92, a child psychiatrist with a Massachusetts-based private practice, knows a thing or two about how to prepare for challenges. A member of the U.S. National Rowing Team in 1992 and 1993, Remmler and her rowing partner won a bronze medal in the lightweight women's double sculls event at the World Championships in 1992.

Remmler, who is still at the top of her game, agrees that focusing on what you can control is key: "I think sports and games or skill-based activities—art, dance, playing a musical instrument—all require a good deal of practice. And undertaking that essential practice is something you can control. You can do the work and push yourself harder, and it has an impact on the outcome. It doesn't mean that you will always win, but it does mean that you are doing what you need to do to win."

One thing that elite athletes are taking more control of is their mental preparation, a tactic that can include working with sport psychologists and specially trained coaches. Sport psychologists and an increasing

number of coaches use techniques such as visualization, meditation, and a mind-body approach known as the personality parts approach, which combines self-talk, meditation and relaxation, and goal-setting. Mikaela Shiffrin, who won a gold medal in women's slalom at this year's Olympic Games, prefers visualization, saying in an interview that she'd turned over in her mind every circumstance, every impediment, every mistake so many times that what everyone else considered to be her first Olympics, was, for her, her thousandth.

Techniques and approaches to enhance performance in competition can help athletes overcome their mind's reactions to the risks, fears, and tensions related to competition and maintain their concentration amid distractions. Attaining an optimal performance state—when the physical and the mental come together seamlessly—is the goal of, and can be the reward for, paying close attention to the power of an aware mind. This state, also referred to as flow or being in the zone, can include perceptual changes such as time seeming to slow; heightened concentration;

dissociation from distractions; greater tolerance of pain; and a feeling of transcendence. Some athletes say that after their best performances they remember almost nothing of their actions; they were able to so fully immerse themselves in the experience of competition that they succeeded in shutting out everything except the task at hand.

On Hold

Some challenges present themselves before a competition, and sometimes they come from within. Athletes want to understand these inner reactions and learn what to do with them. In his work with athletes, John Livingstone '58, an HMS assistant clinical professor of psychiatry at McLean Hospital, finds that intrusive thoughts, such as being concerned about letting down your team or being out of shape; emotions like dread and overexcitement; and bodily sensations, such as "butterflies" in the stomach, commonly take over athletes. These reactions, which are collectively known as "pop-ups," can be triggered by events, relationships, perceived slights from coaches or teammates, or the



stress hormones, such as cortisol; it allows a pop-up to reappear in the next competition; and it prevents athletes from learning from their reactions. Practicing this kind of engagement, he notes, helps an athlete tolerate difficult emotions and pain.

Livingstone, himself a dedicated rower and a mind-body athletic coach, has adapted for sports the internal family system psychotherapy concept of working with personality parts, an approach that differs considerably from positive self-talk and meditation. He notes that research has found that athletes who explore their inner reactions not only learn more about themselves, they also develop lifelong skills for handling intrusive mental experiences.

Coach Class

Another view of how to cope, especially with an off performance, is provided by Richard Ginsburg, an HMS assistant clinical professor of psychology at Massachusetts General Hospital and co-director of the MGH PACES Institute of Sport Psychology, who points to the potential benefits of failure. There is research, he says, indicating that we learn more from our failures and that the brain “grows more from failure than it does from success.”

Gaining the ability to cope with the ups and downs of performance, athletic or artistic, can start early. The psychological development of an athlete may, in fact, have an analogy in child development, particularly when compared with the concept of play, or recreation. Citing the work of Donald Winnicott, a renowned child psychiatrist who did most of his work in the 1940s and 1950s in England, Remmller talks about “the idea of the transitional space, which takes place for people when they’re engaged in an artistic or creative process. And you may not think of rowing as creative or artistic, but racing most certainly is. Racing is a performance which requires you to use your developed skills while being attuned with your instincts.”

Winnicott’s concept of transitional space, says Remmller, can be loosely defined as the space where boundaries between reality and fantasy dissolve slightly, where an individual has an opportunity to move from what she was into what she can become. It is, she adds, “a place where one can express one’s ‘best’ self.”

In athletics, this opportunity to move toward one’s full potential depends on experiencing situations that lead to trust;

sum of an athlete’s experiences. The agendas of the pop-ups may be in conflict, says Livingstone, and, if not handled well, can hijack the mind and body and compromise an athlete’s concentration and muscular performance.

Livingstone draws upon evidence-based methods to teach coaches to help athletes understand that they can soften these reactions by saying, “I am listening to you. I’m curious, and I’ll get back to you later.” He adds, “Athletes need to appreciate that these pop-ups are only a part of themselves. This appreciation frees them to focus on their sports.”

To athletes he works with, Livingstone recommends that, after clearing themselves of an interfering pop-up, they revisit the reaction soon and spend about 15 minutes exploring the feeling and belief behind it. There is evidence, he says, that this second step leads to a more permanent change in the competitor’s inner world. Past practice has been to ignore and bury intruding thoughts, but pushing down these mental intrusions has disadvantages: it stimulates production of performance-compromising

for instance, practice sessions that lead to an athlete’s trust in her ability to perform and to an understanding of how she will react during competition. Winnicott notes that this evolution works best when a trusted friend, therapist—or coach, in this context—gives the individual—the athlete—positive feedback.

Ginsburg sees the search for self through sports develop in children from an early age, saying that “for children between the ages of 6 and 12, the focus is on building relationships and skills, and on developing a sense of belief in their own abilities, how to play a sport and be part of a team.” Later, adolescents start to “learn to work through adversity in a relatively benign setting like athletics.” According to Ginsburg, participating in sports will naturally lead to disappointments and conflicts. But those experiences can foster an ability to deal with conflict and to work with others toward a common goal. “It’s sort of the playground for all of life’s issues,” he adds.

Echoing Winnicott’s thoughts on the role a trusted person can have in an individual’s development, Ginsburg says that a coach can help young athletes focus on questions such as “How did we play? Did we play the style we like to play? Are we working well together as a team? Are we never giving up? If we do those things, it doesn’t matter what happens on the scoreboard.”

Remmller says that coaching comes down to having “coaches who have confidence in you, one who can convince you that they believe in you and that you can believe in yourself, too. It’s a lovely relationship when it works well.”

And what’s good for the individual athlete may also be good for the team athlete. Livingstone says that “being a good teammate means being in ‘self energy,’ not being hijacked by a fear of competition. This applies to the individual athlete as well—knowing yourself and thus the kinds of preparation and coping strategies that will work for you.”

While team athletes draw on the energy of their teammates, individual athletes often field their own internal team, working on Berra’s “half mental” part of preparation by carrying in their minds the people who believe in them and the people they love and admire, each reminding them of their true selves as they flow. ■

Susan Karcz is assistant editor of Harvard Medicine magazine.

PRIMA. CAP. SECUNDA. TERTIA.
XXXI FIGURA.



QVINTA · SEXTA · SEPTIMA ·

XXXI.

QVARTA*



OCTAVA*

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structural elements

Orthopedists tap improved imaging, bioregeneration, and less-invasive surgeries to help athletes mend

A young woman lies anesthetized on the operating table. Sterile blue drapes expose her left knee, tea-stained with antiseptic and swollen with saline. ■ A few weeks ago while running across a soccer field, she planted her cleat in the turf to change direction. Her knee twisted, and, with a pop, her anterior cruciate ligament tore. At that moment, she became one of the estimated 150,000 people in this country each year who rupture an ACL.

by Stephanie Dutchen



On this wintry day, Elizabeth Matzkin, an HMS assistant professor of orthopedic surgery and surgical director of women's musculoskeletal health at Brigham and Women's Hospital, is surgically reconstructing this patient's torn ACL. Through one of two small holes bracketing the kneecap, Matzkin has inserted a slim tubular camera, an arthroscope, that is transmitting images of her movements inside the joint to a monitor mounted above the table. Through the other opening, Matzkin wields a succession of slender instruments that click, whirr, and whine. Separately, she snips free a pair of hamstring tendons and sews them together to make a new ligament.

Matzkin divides her attention between the knee and the monitor. Nudging a drill into place, she prepares a small pilot hole,

then bores a tunnel for the new ligament, first through the femur, then through the tibia. She threads in the new ACL and fixes it in place at both ends.

"Women tend to have smaller femurs than men. This technique allows me to ensure I have a long enough tunnel for the new ligament," says Matzkin. The minimally invasive technique produces smaller scars and may also allow for a speedier recovery than traditional surgery—this young woman could be scoring goals again within a year.

Tactical Changes

A future version of this procedure may be quite different. In that reality, Matzkin no longer needs to repurpose a hamstring tendon; her colleague has used the patient's own stem cells to grow a new ACL. Matzkin

Minimally invasive techniques continue to be game changers in sports medicine.

also no longer worries about her patient developing arthritis. Scientists have figured out how to preserve cartilage and prevent joints from degenerating. And Matzkin no longer sees this injury more frequently in women than in men. After researchers discovered why female athletes tore their ACL two to eight times more often than male athletes—and disproportionately suffered certain other physical injuries—athletes and trainers used that new knowledge to close the gender gap through education and prevention.

According to Jesse Jupiter, HMS Hansjörg Wyss AO Professor of Orthopedic Surgery at Massachusetts General Hospital, studies are underway in each of these areas. In the laboratory, researchers are growing tendons from stem or tendon cells. Surgeons have begun to transfer cartilage cells from inside a knee or an ankle to parts of a joint that have lost their gliding cushion.

"Thirty years ago, football players who tore their knees needed open surgery," says Jupiter. "Those guys now have permanent disabilities. Today, we not only can repair torn tissue and cartilage, we've got office arthroscopy with local anesthesia that provides a quick sense of what's going on in the joint."

Minimally invasive techniques continue to be game changers in sports medicine. Rather than making a wide incision to insert a plate and screws to stabilize a cyclist's broken collarbone, surgeons can now insert a metal rod through a small opening. Doctors are using ultrasound probes to stimulate tendon healing in patients with tennis elbow, thus offering treatment that's less aggressive than standard injection techniques.

Improved imaging helps, too. Enhancements in diagnostic imaging mean that orthopedists can quickly receive images pinpointing the location and detailing the extent of an injury. Researchers are assessing new magnetic resonance techniques to uncover spinal conditions, peer inside joints, and measure tissue stiffness at trigger points, the painful spots of hyperirritated muscle that arise from trauma-induced musculoskeletal stress. Musculoskeletal ultrasound offers a new way to diagnose injuries and to study changes in inflammation or blood flow immediately after an activity.

Real-time imaging allows physicians to see whether they're targeting the right spot

Research has shown that athletes at all levels can lessen the likelihood and severity of injury by staying fit, even in the off-season.

during treatment. Rosalyn Nguyen, an HMS instructor in the Department of Physical Medicine and Rehabilitation at Mass General and Spaulding Rehabilitation Hospital, is using ultrasound to guide injections given to alleviate joint pain. She says the exceptional level of control she gets by holding the ultrasound wand in one hand, watching the screen, and manipulating the syringe in her other hand is worth the years it can take to master the technique.

"It helps me improve accuracy and therefore efficacy, especially for patients who haven't responded to previous injections," she says.

The Next Generation

Advances are not found only in the clinic and the surgical theater. Research has shown that athletes at all levels can lessen both the likelihood and severity of injury



“My patient may be a celebrity, but he’s also somebody’s son,” says Jesse Jupiter, who last year performed multiple arm surgeries on New England Patriots’ tight end Rob Gronkowski. “I want to treat him as responsibly as if he were my son.”



by staying fit, even in the off-season. And athletes and their trainers are analyzing and optimizing the biomechanics behind certain sports—how a golfer swings or a how a pitcher throws a softball—to avoid overuse injury or prevent reinjury.

Even with improvements like these, many people with sports-related injuries to their bones, muscles, tendons, or ligaments don't heal as well as they could. For them, hope lies in the burgeoning field of bioregenerative medicine. In this discipline, researchers are developing ways to replace or regrow damaged tissues by stimulating the body's natural healing abilities.

One technique that has generated interest is the injection of fluids to stimulate healing. This may involve the use of platelet-rich plasma, or PRP, filtered from the injured athlete's blood. Another approach, known as proliferative injection therapy or prolotherapy, calls for the injection of a mild irritant, such as a dextrose solution, to stimulate healing.

"It's like recruiting the patient's warrior cells to an area," says Nguyen, who performs both procedures. "They marshal other cells to the region and take the patient through the stages of the healing cascade: inflammation, proliferation, remodeling."

Clinical trials are underway, and early research suggests that PRP and prolotherapy reduce pain and hasten recovery in athletes with certain tendon, ligament, and joint injuries—including rotator cuff tendinopathy, tennis elbow, and plantar fasciitis—who have not responded to other treatments or who want to avoid surgery.

New techniques being explored by Jupiter and other researchers involve using an athlete's mesenchymal stem cells—young cells that can become a variety of cell types, including bone, cartilage, or fat—to mend broken bones, restore arthritic joints, or grow new ligaments.

Currently, 5 to 10 percent of patients have fractures that fail to knit back together in under nine months. For those patients, physicians rely on scaffolds, bone grafts, cement, and other mechanical remedies. Jupiter believes that adding mesenchymal stem cells to those techniques might help stimulate the blood flow and bone growth necessary for healing.

He imagines one day implanting a tube seeded with stem cells and growth factors into the injured area, triggering the body to make its own new bone, or elastic ligament, or gliding cartilage.

Currently, 5 to 10 percent of patients have fractures that fail to knit back together in under nine months.

The X Factor

Not all advances are technological. Some involve understanding the needs of special populations.

Although 42 years have passed since Title IX ushered in a flood of female athletes at colleges and universities, there are still gaps in our understanding of the extent to which women's injuries differ in location, frequency, presentation, and severity from those of men in the same sport. Journals teem with studies attempting to identify the components: When is anatomy to blame, like women's smaller ACL notches, wider pelvises, or more "knock-kneed" stance? What roles do hormones play in collagen, bone, and ligament characteristics? Does strength and movement training reduce injury? The answer to the last one, happily, appears to be "yes."

As director of the Women's Sports Medicine Program at Brigham and Women's, as well as physician to several national and collegiate women's sports teams, Matzkin has a front-row seat to the factors that affect female athletes. Chief among them is a cluster of interrelated conditions known as the female athlete triad. First defined in 1992, it consists of poor nutrition, menstrual irregularities, and low bone density. Women with the triad fall along a spectrum of not eating three balanced meals a day to full-blown anorexia or bulimia.

"The resulting low energy balance throws off their systems so they don't get their menstrual cycles regularly," Matzkin says. "That's bad for the bone health of young women—particularly since they're at the age

when the bone density they build is all they're going to have for the rest of their lives."

Other researchers have focused on women who are pregnant and who want to continue to be physically active. In the past few decades, studies have demonstrated the health benefits and low risks of physical activity for both mother and fetus, convincing orthopedists to encourage moderate, noncontact exercise during and after pregnancy. Specific guidance is taking shape for gestational diabetes and high blood pressure.

Back in Play

Orthopedists who specialize in sports medicine tend to share certain characteristics with their patients: They love sports, they're team players, and they want to perform to the best of their ability. They also value a level playing field.

For Matzkin, Nguyen, and Jupiter, a six-year-old who falls while ice skating receives the same care as a shortstop who sprains an ankle in a playoff game. The professional athlete simply comes with a larger crowd—coach, trainer, agent, media, fans—whose pressures a doctor must weigh against the medical evidence of the player's recovery.

"My patient may be a celebrity, but he's also somebody's son," says Jupiter, who last year performed multiple arm surgeries on New England Patriots' tight end Rob Gronkowski. "I want to treat him as responsibly as if he were my son."

And like parents, orthopedists take pride in seeing their patients get back in the game.

"As a surgeon, I love operating. But more than that, I love seeing patients return to what they want to do when they're recovered," says Matzkin, pointing to postcards and newspaper clippings sent by former patients eager to share their varsity game scores or snapshots of them hitting the slopes again. "Working with athletes is great. They're very motivated to get back to being active."

As children engage in single sports more intensely and older adults become more active, as women and men of all ages commit to club sports and recreational activities with as much passion as professional athletes, orthopedists who seek out and apply the latest advances will continue to serve as invaluable members of the team. ■

Stephanie Dutchen is a science writer in the HMS Office of Communications and External Relations.



Boston's teams draft local talent

HOME TEAM

R. Bruce Donoff

Position: Attending Oral Surgeon

Team: Boston Bruins

RUMINATING OVER AN OLD PHOTOGRAPH hung on a wall in his office, R. Bruce Donoff '73, dean of the Harvard School of Dental Medicine, projects a calm gentleness that one might not associate with the rough and tumble of a professional ice hockey team. Yet the oral and maxillofacial surgeon has consulted with the Boston Bruins for nearly two decades.

"Dr. Donoff, thanks for all your help," he says, reading aloud the inscription below the picture. "This was taken in the old Boston Garden," he adds. "That long ago."

Donoff, who also is the School's Walter C. Guralnick Distinguished Professor of Oral and Maxillofacial Surgery, says that the health care provided for professional hockey players has much improved since he became involved with the sport. A good deal of that improvement came as a result of changes following the strike by National Hockey League players in the early 1990s. Among its stipulations, the contract settlement mandated that a team physician and dentist be present at every game.

In need of a dentist who could handle both the volume and variety of dental and jaw injuries, the Boston Bruins searched for an oral and maxillofacial surgeon. Donoff was approached by Ashby Moncure, a surgeon at Massachusetts General Hospital who was working with the Bruins at the time. Could Donoff provide dental coverage to the team? "I'd taken care of a lot of fellows with broken jaws," Donoff says. "That's really how I got into it," he adds.

Donoff treated injuries ranging from broken bones to lacerated lips, and teeth that had been displaced from their sockets. He also began making bite guards for the players, which is now done routinely, but was not then standard practice.

"I joke that I could tell the quality of the season by the number of fractured bones the players had," he says, equating more aggressive play to better performance. He notes that players, once proud of their missing teeth, have become more "cosmetically conscious" in the past decade or so.

"Talk about a sign of the times: I was at a Bruins-Rangers game, and one of the New York Rangers took a puck in the lip. I got called down to sew it up. As I began to sew up his lip, he said, 'Doc, how are my veneers?' I said, 'Veneers?'" Donoff laughs. "Hockey players usually don't have veneers. So they've gone from being proud of their missing teeth to being cosmetically conscious. What can I say?"

Donoff has treated his fair share of celebrated athletes; for example, he fixed the jaw of Stanley Cup winner Ray Bourke. He notes that, over the years, the players have gotten bigger and, consequently, the hits have gotten harder. Although he still enjoys watching the Bruins compete, and receives tickets to the games from some of his former patients, he chuckles as he reveals a little secret: the best seats are at home.

with care by Valerie Wencis

JOHN SOARES



George Theodore

**Position: Orthopedic Surgeon/
Foot and Ankle Consultant
Team: New England Patriots**

THE TWO MEN TALKING about New England Patriots' tight end Rob Gronkowski's injury had no idea that the man next to them was the orthopedic surgeon who had worked on that famous ankle. George Theodore '91 recalls this conversation with amusement, just one of many he's overheard while out and about in Boston. Does he ever volunteer his part of the Gronkowski story? He shrugs, "I prefer to keep a low profile and let the outcomes speak for themselves."

This appears to be a good strategy for Theodore, who serves as a foot and ankle consultant for New England's professional baseball, football, hockey, and soccer teams and also tends to the injuries of professional athletes from teams outside of the region. Theodore, an HMS instructor in orthopaedic surgery at Massachusetts General Hospital, sees sports icons at their most vulnerable, helps them work through their concerns and injuries, and, fortunately, as he notes, is often able to celebrate with them when they recover.

"I treat my athlete patients as I treat all my patients. I extend to them the same kindness, sensitivity for their injury, and devotion to their care," he says.

Theodore considers it a privilege to be a surgeon who has helped professional athletes overcome injury, including most valuable players (MVPs) from two different sports: Tom Brady of the Patriots and Dustin Pedroia of the Boston Red Sox. He also acknowledges the pressure that comes with treating such high-profile patients. "Their careers, their lifestyles, their sources of income, everything that forms their professional lives, could depend on whether their surgery goes well," he says. "But there's also a lot of satisfaction in knowing they place their trust in me as their doctor to get them back onto the field."

This former Harvard College classics major hadn't set out to become an orthopedic surgeon, but elected to specialize in the field when he realized what an effect orthopedic surgery could have on someone's life. "I thought it was a well-defined field that allowed you to help everyone: young, old, male, female, super athlete, and couch potato." And he's done just that. Reflecting on his career, Theodore says, "I'm lucky. I'm blessed."

Valerie Wencis is associate director of communications in the HMS Office of Communications and External Relations.



Laurence Ronan

Position: Medical Director/Internist
Team: Boston Red Sox

LAURENCE RONAN '87 is dedicated to knitting together lives disrupted by injury and trauma. That resolve often puts Ronan, head of the Thomas S. Durant Fellowship for Refugee Medicine at Massachusetts General Hospital and an HMS instructor in medicine, at the site of national and international disasters, directing relief efforts in such places as New Orleans, Haiti, Indonesia, and Iraq. In Boston, that commitment drives the care he provides to his patients at Mass General. Since 2005, that

same commitment has guided the medical care he provides to the players on Boston's baseball team, the Red Sox.

This last responsibility might seem unexpected. It is to Ronan. Although he has always been interested in sports—growing up, he wrestled and played baseball, basketball, and football—Ronan never imagined he would one day serve as a physician for a professional sports team. The experience has taught him that athletes are like all patients. They have aches and pains. They also don't like to let illness or injury hold them back.

"These are competitive people. They want to be in the game all the time. It's a bit of a task to try to make that work for them. But the idea always is to get them to a place where they can regain their health and their ability to perform at their peak."

Although Ronan has treated the types of injuries he thought he would—concussions and musculoskeletal and soft-tissue injuries—he had not expected to be confronted with serious disease, such as pitcher Jon Lester's lymphoma. "It's unusual to have a high-performing professional athlete get a serious disease. I watched him go through diagnosis and treatment, and rebuild his body and recover emotionally." As a physician, Ronan saw Lester's trajectory as both heroic and instructive. Today, Lester works with pediatric cancer patients. "He's a really great role model for a lot of our kids with disabilities or who are facing cancer."

One of Ronan's challenges since starting with the Sox has been shifting from the hospital's calendar to the team's. "You go from February through October," he says. "But in the off-season, there's also the draft." Ronan is with the team for four of their six weeks of training each spring in Florida and attends a majority of the home games. "You should talk with my wife," he jokes, noting how much time he and his family spend at the games.

Sports medicine as a whole has changed, Ronan says. At Mass General, it has evolved from a sports orthopedic service to a multidisciplinary team that includes surgeons, internists, nutritionists, physical therapists, psychologists, primary care sports medicine doctors, and cardiologists. "We do a lot of research on heart, endocrine, and bone issues that affect athletes," he says, "as well as on musculoskeletal and soft-tissue concerns. I've appreciated being a part of this larger group of sports medicine professionals." ■

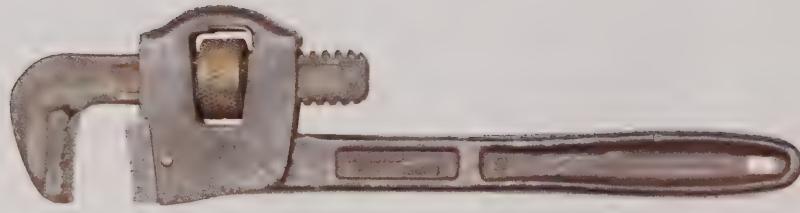


CENTER OF ATTENTION: Throughout his tenure as director of the Harvard Medical Unit at Boston City Hospital, William Bosworth Castle (center) was appreciated for the time he spent as teacher and mentor to the hospital's medical staff and faculty.

AT THEIR

The Harvard Medical Unit
created leaders in medicine,
leaving a legacy of world-
class teaching, research,
and patient care
by Debra Bradley Ruder

SERVICE



In August 1949, on a day when the temperature simmered around 105°F, Edward Kass climbed the stairs of the Thorndike Memorial Laboratory. He would soon begin a fellowship there in infectious diseases. Upon reaching the fourth floor of the Harvard Medical School-led clinical research center at Boston City Hospital, Kass was startled to find his mentor, Maxwell Finland '26, at the bench, bare-chested and sweat-soaked. The brilliant scientist was going through stacks of cards that contained sensitivity data on various antimicrobial drugs.

"I asked him why he was working on such a miserable day," Kass recalled years later, "and he responded, in characteristic fashion, that the only way to keep one's mind off the weather was to immerse oneself in work."

That sense of purpose fueled Finland's extraordinary career as an infectious disease researcher and permeated what was then known as the Harvard Medical Unit at Boston City Hospital, a world-class program of teaching, research, and patient care that thrived from the mid-1920s

through the mid-1970s. It comprised two patient-care services and the research activities of the Thorndike.

The unit was a magnet for physician-scientists eager to train with medical giants such as Finland, William Bosworth Castle '21, Sidney Ingbar '47, and James Jandl '49. Its researchers had a profound influence on medicine, yielding early discoveries on infections, blood disorders, diabetes, liver diseases, and other conditions that sickened Boston City patients.

"There was an excitement and a sense of unlimited potential in the atmosphere," wrote Kass, an epidemiologist who spent nearly 30 years at Boston City and was the School's William Ellery Channing Professor of Medicine until shortly before his death in 1990. According to many who participated in it, the program fostered curiosity, imagination, precision, intellectual rigor, camaraderie, and pride. All that within the confines of an underfunded, overcrowded hospital with broken plumbing, supply shortages, and the grinding reality of poverty.



Goodwill to All

HMS had served Boston City since the hospital's founding in the South End in 1864, but the School's role expanded in the 1920s with the appointment of Francis Weld Peabody, Class of 1907, to lead its efforts there and to spearhead the construction of the Thorndike Lab, the first clinical research center in a U.S. municipal hospital. Named for surgeon William Thorndike, Class of 1848, the center housed a 17-bed ward for clinical research and two floors for laboratory investigations.

For years, Boston City was affiliated with Harvard, Boston University, and Tufts Medical Schools and was widely acknowledged as a stimulating environment for clinical research, patient care, and medical education. During the pre-Medicare era, the hospital attracted "some of the sickest, poorest, saddest, and often drunkest people you can imagine," notes Daniel Federman '53, HMS Carl W. Walter Distinguished Professor of Medicine. Patients didn't know how long they'd wait, but once seen, "they knew they would receive some of the kindest, most loving, most dedicated care on Earth."

The Harvard Medical Unit drew students, postgraduate trainees in internal medicine, and fellows focused on clinical subspecialties and medical research. What is remembered as a glorious tradition, however, ended in the early 1970s when hospital trustees, facing financial pressures and a falling patient census, decided to affiliate with BU only. Eventually the hospital was renamed Boston Medical Center.

But the Harvard program's legacy endures: Many members have assumed leadership roles, earning positions as professors, department chairs, and deans in Boston and beyond, training new generations of physician-scientists along the way. And the names of the unit's luminaries are attached to HMS professorships, student societies, and an annual event celebrating student research: Soma Weiss Day.

Well Springs

Advances in medicine sprang from the work of Thorndike investigators. They were a remarkably productive group, publishing nearly 100 papers during the four years before Peabody's death in 1927 and roughly 100 papers a year during the tenures of subsequent directors George Minot, Class of 1912, and Castle. Many studies were based on clinical observations, but basic research and animal experiments also took place.

Thorndike's research divisions, formed in the 1950s, embraced investigators who spurred progress in hematology, cardiology, infectious diseases, endocrinology, diabetes, gastroenterology, pulmonary diseases, and nephrology—and later, as medicine evolved, in genetics and other areas.

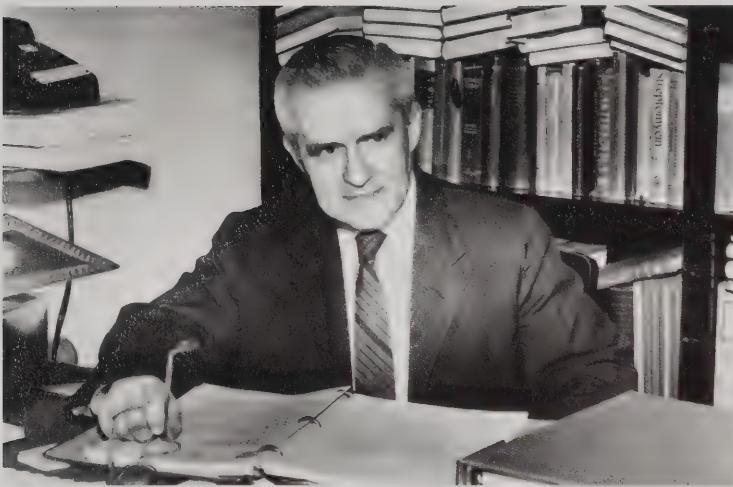
Finland and his infectious diseases group conducted seminal work on pneumonia, antibiotics, and hospital-acquired infections.

This included rigorous studies of the efficacy and side effects of almost every antibiotic developed between the late 1930s and the 1970s, among them sulfonamides and penicillin. Finland's team also documented the emergence of antibiotic-resistant bacterial organisms—in particular, gram-negative bacilli and *Staphylococcus aureus*—and their role in causing serious infections in patients at Boston City.

Considered the birthplace of modern hematology, the Thorndike produced crucial insights into the pathophysiology of anemia, the destruction of red blood cells and platelets, the nature of hemoglobin in normal and sickle cells, therapies for hemophilia, and classifications of lymphomas based on cell morphology. In addition, Thorndike researchers discovered that a diet rich in vitamin B12 could successfully thwart pernicious anemia, which, at the time, was a



STRIKE A POSE: George Minot (far left), who followed Francis Peabody as director of the Harvard Medical Unit, stands with Edwin Allen Locke, a Boston City Hospital physician. At right, technicians Sylvia Warren (seated) and Olivia Ames volunteered in the Hematology Division of Thorndike Laboratory in the 1920s.



fatal disease affecting 1 to 2 percent of adults over age 50. Minot and William Murphy '20 shared the 1934 Nobel Prize in Physiology or Medicine for this work with George Whipple of the University of Rochester. Castle extended these findings through years of study on the biological causes of pernicious anemia. As a resident, he ingested and regurgitated hamburger meat that was then fed to patients through a nasogastric tube, a clever, and, by today's standards, alarming experiment that demonstrated the existence of an intrinsic factor necessary for the body's absorption of vitamin B12.

Castle wasn't alone in volunteering himself for research. Years later, physician Victor Herbert set out to examine folate behavior in adults by eliminating the vitamin from his diet. Ronald Arky, a Thorndike fellow in the 1960s and early 1970s who studied diabetes and metabolism, recalls the effects of that self-study, "On Christmas Day in 1961, I came into the Thorndike building and found Victor, so weak he didn't have the strength to push the elevator button." Arky is now the Daniel D. Federman Professor of Medicine and Medical Education and master of the School's Francis Weld Peabody Society.

The School's research enterprise at Boston City expanded in the early 1960s with the construction of the Channing Laboratory. Led for years by Kass and now part of Brigham and Women's Hospital, Channing is a locus for research on infectious diseases and epidemiology. The Nurses' Health Study was begun in 1976 by longtime lab member Frank Speizer, now the HMS Edward H. Kass Distinguished Professor of Medicine, when he headed Channing's clinical epidemiology division.

Among other accomplishments of Channing investigators are studies that

advanced the diagnosis and treatment of urinary tract infections. A team led by Kass in the mid-1980s found that toxic shock syndrome, a rare but debilitating, and sometimes fatal, bacterial infection, was triggered by magnesium deficiency, an imbalance that occurred when the mineral was absorbed from the body by fibers in certain tampons. Channing scientists also helped launch the East Boston Neighborhood Health Center, which was directed for more than 40 years by chronic disease epidemiologist James Taylor, and which remains one of the nation's most successful community health centers.

Lunch Bunch

What made the Harvard Medical Unit unusual? Former trainees and faculty point to the collaborative atmosphere, high expectations, and exceptional colleagues, nurses, technicians, office staff, and patients.

"We all spoke to one another in those days," says Harry Jacob '58, an intern and fellow from 1958 to 1969, who went on to head the Division of Hematology/Oncology/Bone Marrow Transplant at the University of Minnesota for nearly four decades.

"The lunchroom tables were always shared by a mixture of Thorndikers, house staff, and faculty from the three universities teaching at Boston City," he adds. "Conversation was brisk, funny, and, uncannily, almost always engendered new ideas for laboratory research."

"I've never run into a spirit of free inquiry and conviviality that matches what we had at the Thorndike during those happy years," wrote hematologist H. Franklin Bunn, who was at Thorndike between 1964 and 1974 and is now an HMS professor of medicine

When something went wrong with a sink, word went back to Castle, and the next morning you'd see this world-renowned physician-scientist under the sink fixing a drain pipe.

in the Hematology Division at Brigham and Women's. Bunn's lab identified the structure and biosynthesis of hemoglobin Alc, now used worldwide for diagnosing and monitoring patients with diabetes. Mentors were supportive but demanding, Bunn adds. Research out of Thorndike dominated annual meetings on clinical investigation "because the quality of the work was remarkable. We had elaborate rehearsals, and the presentations were first-rate."

One of the more admired mentors was Castle, who led the program between 1940 and 1963 and often chaired Saturday morning rounds, which brought in well-known physicians to discuss clinical problems. Warm, witty, and generous with his time, Castle was a father figure to many, often



INSTITUTIONAL MEMORIES: Maxwell Finland (far left), who directed the Harvard unit in the 1960s, wrote a three-volume history of the program at Boston City Hospital (center, circa 1920) and of the research conducted there, at the Channing Laboratory, and at the Thorndike Laboratory (above, circa 1970).

seeking the views of medical students, residents, and fellows on topics in biology that interested him. He loved to tinker and kept a wooden toolbox on hand in case radiators or plumbing needed repair. "When something went wrong with a sink, word went back to Castle, and the next morning you'd see this world-renowned physician-scientist under the sink fixing a drain pipe," recalls Neal Steigbigel '60, a house officer and fellow in the 1960s who went on to lead the Division of Infectious Diseases at Montefiore Medical Center in New York for three decades.

Finland, meanwhile, was known for his devotion to Boston City, where he spent most of his career, serving as an intern in the 1920s and directing the Harvard Medical Unit in the 1960s. He retired in 1968 as the George Richards Minot Professor of Medicine Emeritus, but remained at the Thorndike until the early 1980s.

Although always ready to provide advice and support to his Thorndike family, Finland "wasn't a great lecturer," says Steigbigel, "but if you asked him questions—and he particularly loved to be asked at irregular hours because it showed you were devoted to your job—he would wax eloquent on favorite subjects, such as pneumonia. He'd pull out papers and discuss them in a collegial, scholarly, and critical manner. Max was short in stature but huge in intellect and heart." In his later years, Finland poured his energy into producing a three-volume history of the Harvard program, published in the early 1980s.

Another beloved mentor was Charles Davidson, the William Bosworth Castle Professor of Medicine, who served Boston City for three decades starting in the 1940s, and who studied cirrhosis, alcoholic

hepatitis, and related diseases. He also began the morning report tradition for house staff. Former resident Walter Willett, an HMS professor of medicine and the Fredrick John Stare Professor of Epidemiology and Nutrition at the Harvard School of Public Health, credits Davidson with encouraging his interest in the association between diet, health, and disease. Joining Boston City "was a real turning point in my life," Willett notes. "It never would have happened had Charlie Davidson not led me around the dark corridors and passageways with such enthusiasm that I knew there had to be something special about the place."

Premium Care

Faculty and trainees alike were guided by Peabody's philosophy of respectful and compassionate care, articulated in his famous 1925 essay, "The Care of the Patient," which is still distributed to HMS students. "One of the essential qualities of the clinician is interest in humanity," Peabody stated, "for the secret of the care of the patient is in caring for the patient."

Boston City patients often had multiple problems linked to poverty and alcoholism—malnutrition, diabetes, liver disease, bacterial pneumonia, and meningitis, for example—and were seen both on wards and in outpatient clinics. HMS physicians also handled emergencies, including helping hundreds of victims after the horrific Cocoanut Grove nightclub fire in 1942.

Repeat patients often got attached to their doctors, and vice versa. "They were good, decent people; they were part of the family," explains Robert Glickman '64, Robert M. and Mary H. Glickman Professor of Medicine and Gastroenterology at the NYU School of Medicine. Glickman experienced Boston City as an intern and resident. "You tried your best to help. A lot of the patients were very grateful, so it was rewarding."

That gratitude could be expressed in simple but profound ways. "I had one fellow, a regular patient in the outpatient clinic," Steigbigel says, "who brought me a gift around Christmastime one year. I unwrapped the package and found a box of Premium saltine crackers. I was so moved and astounded."

The School's medical services at Boston City attracted self-reliant house officers who could react quickly and creatively to deliver the best possible care under challenging circumstances. "You had to learn things in milliseconds," recalls Peter Tishler, a medical geneticist at Brigham and Women's, who was at Boston City between 1960 and 1977. "It was 'See one. Do one. Teach one.'"

Supplies were scarce, and medical students often "procured" rubber gloves, tourniquets, needles, and other essentials during their rotations at better-equipped hospitals. House staffers were the ultimate do-it-yourselfers, seeing to everything from collecting specimens and delivering them to the lab to transporting patients through the hospital's slippery, inclined tunnels.

Those adventures could be hair-raising, as former resident Matthew Liang '69, now an HMS professor of medicine at Brigham and Women's and the chief of rheumatology at the Boston VA Healthcare System, can attest. He describes ferrying a man with end-stage liver disease and gastrointestinal bleeding along one of the tunnels. The patient weighed at least twice as much as Liang. "I took a running start up a ramp, but I didn't have enough oomph to clear it, and the gurney drifted to the side and hit the wall," he says. "I was helpless to prevent the collision."

For Liang and others on the HMS unit, Boston City forged lifelong memories and connections.

"We all stood on the shoulders of those who came before us," says Speizer, "and we all have tried to convey those lessons to the generations that have followed." ■

Debra Bradley Ruder is a Massachusetts-based education and health care writer.

A Stitch Inside

First comes the pop; then, the pain.

There is little doubt when an anterior cruciate ligament tears, but its inability to mend remains a puzzle, one that Martha Murray is trying to solve.

The ACL forms a fan-shaped bridge vertically spanning the knee's interior and linking the long leg bones above and below the joint. Multiple crisscrossed fibers help stabilize the knee, fine-tuning its motion from within. Twisting and turning—the mainstays of slopestyle skiers, pickup basketball players, and tennis pros—depend on the smooth operation of this ligament.

Left alone, a torn ACL cannot knit itself back together, a fact that Murray, an HMS associate professor of orthopedic surgery at Boston Children's Hospital, found compelling and curious.



After all, ligaments outside the knee can heal. But unlike those neighbors, the ACL is bathed in synovial fluid. The lubricant helps the knee move smoothly, but it also dissolves the blood clots and scar tissue that a ruptured ACL would depend upon to rejoin its two torn ends.

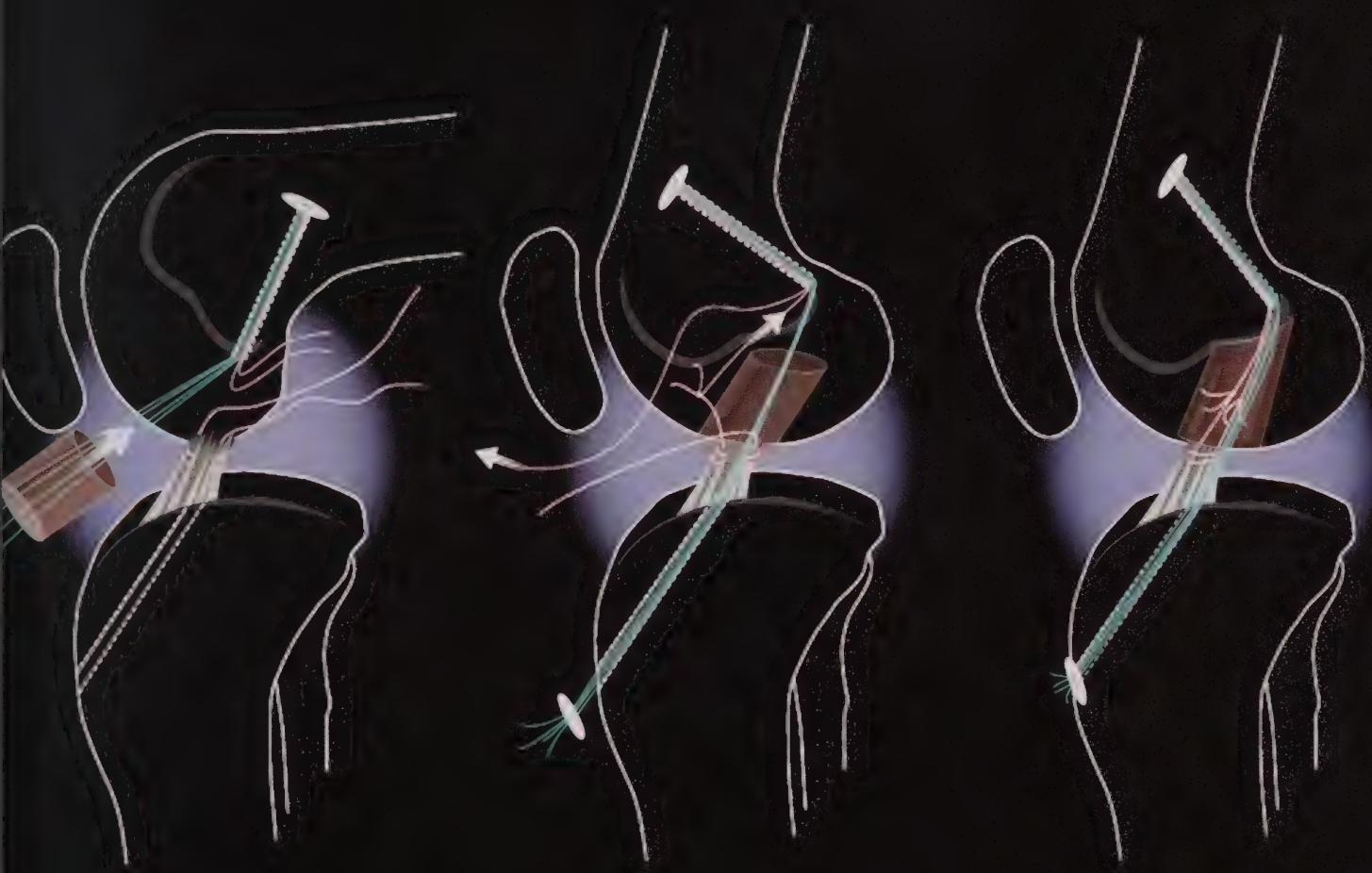
Since the 1970s, surgical reconstruction of the ACL has been the standard of care for such traumas. Instead of sewing the pieces back together, surgeons insert a graft—perhaps part of a

BRIDGE BUILDING:
A technique called **bioenhanced ACL repair** preserves the torn ACL tissue and provides a **collagen scaffold** upon which **cells** can grow to reunite the **sundered ligament**. In this method, the **collagen scaffold** is anchored in place with **sutures**, then **saturated with blood** from the patient. The **collagen-platelet scaffold** then serves as a **substrate** for the **healing** of the torn ligament.

hamstring or a patellar tendon—to reconnect the back of the femur with the front of the tibia. After rehabilitation, patients resume activity, including sports at the Olympic level.

Most people recover well, but not the ones who worry Murray.

The peak age for young women to tear their ACLs is from 15 to 19 years old. But researchers say as many as 30 percent of female soccer players under age 20 who return to the game after an ACL reconstruction will tear



their grafts, compared with 2 percent of adults.

People of all ages face another problem: After an ACL tear, the risk of developing osteoarthritis in the same knee within 15 years is as high as 75 percent. No one knows why.

Murray believes helping the ACL heal is the answer. After two decades of animal research, she has developed a collagen scaffold that helps unite the two stumps of a torn ACL. Infused with ligament proteins and filled

with blood, the tubular scaffold is inserted between the torn ends, stabilizing a biologic bridge where healing can take place. She hopes to soon gain approval for a clinical trial in patients.

"My grandmother used to say, 'Everything is mendable,'" says Murray. "I'm just trying to mess with Mother Nature as little as possible, and provide only what is missing—a stable bridge—and then let the knee work as its own bioreactor."

—Elizabeth Cooney

BACKSTORY

FROM THE COLLECTIONS AT HARVARD MEDICAL SCHOOL

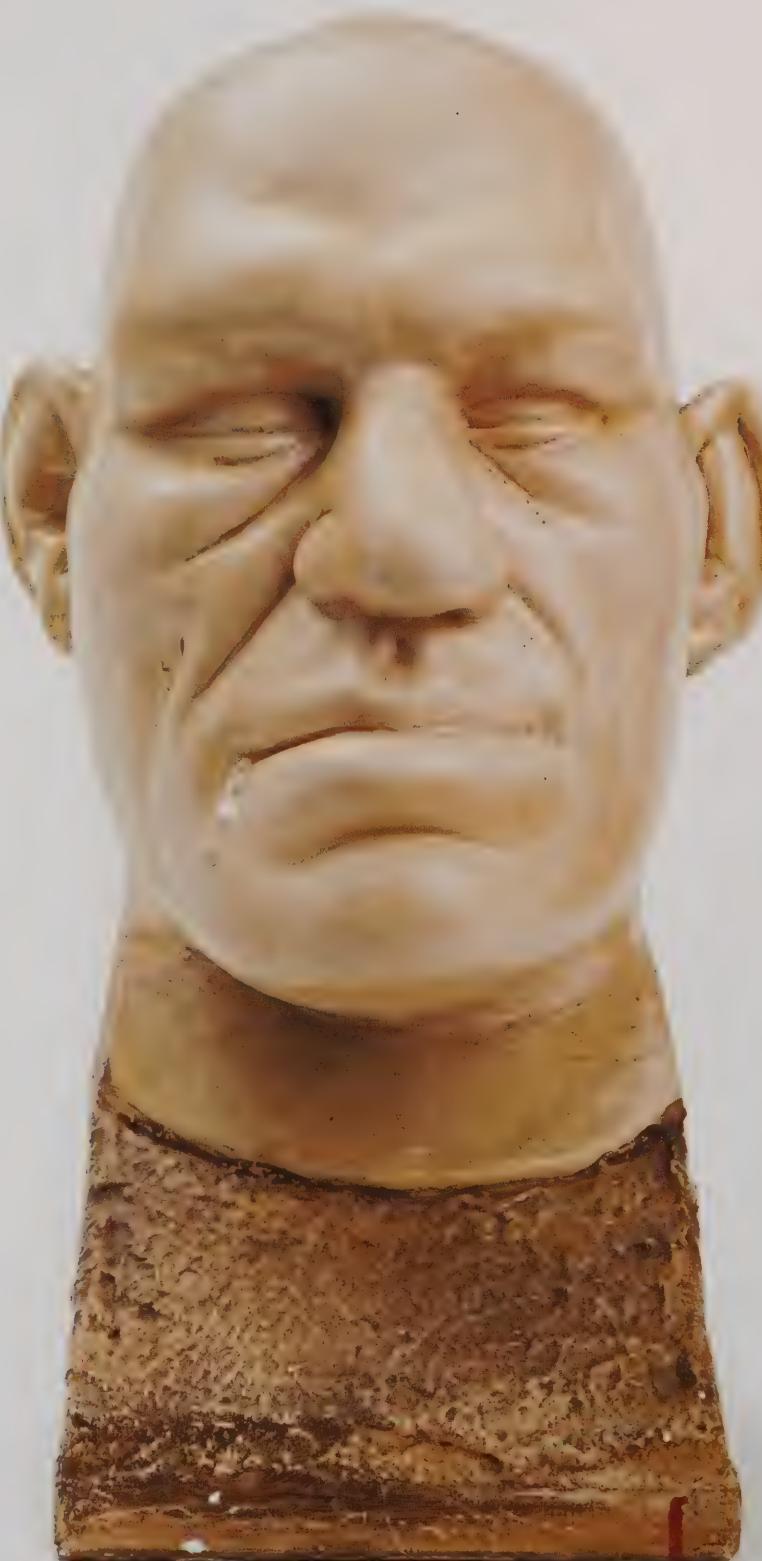
When Paul Dudley White,

Class of 1911, was called in to consult on Dwight D. Eisenhower's medical condition after the president's heart attack, he recommended something that was not, in 1955, the standard of care: exercise.

White knew his business when it came to preventing cardiac disease and caring for heart patients. He began his career at Massachusetts General Hospital in the early 1900s, when cardiology was in its infancy. He was one of the founders of the American Heart Association; he authored *Heart Disease*, the seminal text for the discipline; and, as early as the 1920s, he spoke and wrote about the health benefits of physical activity. His contributions to the field led to White's being regarded as the father of cardiology.

White was an early and strong believer in preventing disease by promoting what is now widely accepted medical advice: eat and drink alcohol in moderation, eschew cigarette smoking, and exercise daily. White himself was an avid cyclist whose legacy includes the Dr. Paul Dudley White Bike Path, a 17-mile loop around the Charles River in Boston.

—Susan Karcz





FUN AND GAMES: Clockwise from top, the chess set carved by Zabdiel Boylston Adams, Class of 1853, and fellow prisoner Fred Guyer during their internment at Libby Prison and their convalescence in a hospital in Lynchburg, Virginia. Both were captains in the Union army, and were injured and captured at the Battle of the Wilderness in May 1864. The Infants Hospital Puzzle and the Intern Game were distributed in 1920 and 1979, respectively. A death mask taken of Maurice Tillet, a professional wrestler of the late 1930s to early 1950s, who was known as "The French Angel." Tillet was remarkable for his large head and oversized facial features, symptoms of the hormone disorder acromegaly.

Chess set, courtesy of the Warren Anatomical Museum at the Francis A. Countway Library of Medicine; game and puzzle, gifts of William H. Helfand, Jr., to the Harvard Medical Library; Tillet mask, a gift of Rosanna Meunier Leonard, Patrick J. Leonard, Sr., Patrick J. Leonard, Jr., and Mary K. Leonard of Braintree, Massachusetts, to the Warren Anatomical Museum.

FIVE QUESTIONS

FOR DAVID GINTY



Why study the sensory neurons of touch?

Touch is a fundamental sense, yet there's so much we don't know about it. We know relatively little about the primary sensory neurons. We know even less about how their projections are organized to give rise to circuits that underlie the perception of touch. And we know very little about how this organization develops. Touch is fascinating and complicated.

Okay, so I'm holding a pen. What do and don't we know about how I accomplish that?

We know your muscles are controlling your gripping of the pen. We don't know the circuits that are mediating the sense of the pen, the force being applied, or the slippage of that pen within your grasp. Presumably there are spinal circuits where those sensory inputs are turned into motor outputs that adjust grip control, but we don't know about the components of those circuits. We don't know how or where information from the different sensory neurons that detect pressure versus stretch versus vibration are integrated to give rise to the perception of your experience of holding that pen.

Describe one avenue you're pursuing.

Given that we have a dozen or more types of sensory neurons, each of which is tuned to different types of stimuli—for instance, some respond best when the skin is indented, others to the stretching of the skin, and others to temperature changes—our thesis is that sensory neurons' activities are integrated in the spinal cord, which then sends integrated information to the brain's somatosensory cortex, where we perceive the nature of the stimulus acting on the skin.

The Edward R. and Anne G. Lefler Professor of Neurobiology, Harvard Medical School

Investigator, Howard Hughes Medical Institute

We're asking how second-order neurons, post-synaptic partners of sensory neurons, and spinal cord interneurons process touch information in the spinal cord, and how that processed information is then sent to the brain.

What motivates you?

We do discovery-based, curiosity-driven research. We're fascinated with how sensory systems develop and function. We're convinced that the knowledge we gain will provide the basis for understanding what happens when things go wrong—and, perhaps, how to fix things.

What do you love about being a scientist?

If, when I was young, I had to say what I would choose as a career, I would have said artist or musician. So I'm lucky; I think being a scientist is a lot like being an artist. Science and art share an open-mindedness and a desire to explore the unknown. In science, as in art, creativity, inquisitiveness, and presentation play huge roles.

I love discovering something beautiful and telling the world about it. In science, when something is discovered and it's right, it's beautiful. And there's no greater joy than describing that beautiful something to the world. It's hard to imagine a more satisfying career.

—Stephanie Dutchen

CONNECT THE DOCS

THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI

President's Report



By now, we've all been touched by the profound transformations occurring in health care. Students

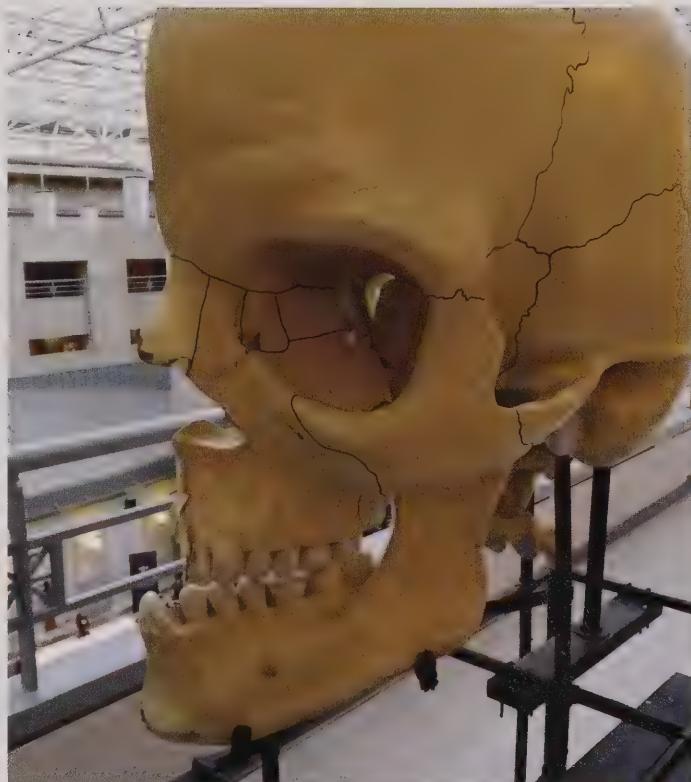
and alumni face many uncertainties, underscoring the need to strengthen our bonds as a community. To meet this need, your Alumni Council has identified several worthy initiatives designed to connect alumni with students, with each other, and with patients in need.

A survey to gauge your thoughts on and interest in these options was part of this year's Alumni Council ballot. Based on your feedback, we hope to launch alumni-student mentorship opportunities, alumni affinity groups, and a project using technology and telemedicine platforms to link volunteers to clinics for the underserved.

We hope you filled out the survey and allowed your voice to be heard. If you did, thanks so much. But if you missed the survey, you may still be able to access it at www.surveymonkey.com/s/alumninvolvement. We look forward to reporting its results in an upcoming issue of *Harvard Medicine* magazine.

Laurie Green '76 is an obstetrician and cofounder of Pacific Women's OB/GYN Medical Group in San Francisco.

SUZANNE SIZER, JAKE MILLER (FAR RIGHT)



MAKE ROOM FOR A BIG, GIANT SKULL

Anatomical models move into new careers

WHEN THOMAS DWIGHT, Class of 1867, succeeded Oliver Wendell Holmes, Class of 1836, as the School's Parkman Professor of Anatomy in 1883, he introduced some big changes: a 60-inch-long skeleton of a foot and a 78-inch-tall model of a sagittal section of a human skull. They could, to be sure, be seen from the back seats of a lecture hall.

For more than a century, those models helped illustrate the nuances of anatomy for HMS students. In November 2013, however, the models

left the classroom behind and became new additions to the collections of historical objects that can be found in the Warren Anatomical Museum at the Francis A. Countway Library of Medicine. They had little time to settle in, as they were soon loaned to the Collection of Historical Scientific Instruments at Harvard University for a public exhibit on the history of human anatomy. A second giant skull, which is dissected transversely, was also commissioned by

Dwight; this model will continue to be used as a teaching aid.

"These were incredible, dynamic education tools, and they should serve as dramatic pieces in what promises to be a powerful exhibit," says Dominic Hall, curator of the Warren Museum. "Afterward, we're hoping we can find a display home for them at the Countway for students' continued interest and reference."

The University's exhibit, scheduled to run from March through December 2014, runs concurrent with one at the Countway. Each highlights many aspects of human anatomy, including its roles in scientific discovery, public spectacle, and medical education.

Objects in the exhibits range from illustrated texts created during the Renaissance by the famous anatomist Andreas Vesalius, to wax-injected limbs of the nineteenth century, to today's digital atlases of the human body, according to David Jones '97. Jones is the A. Bernard Ackerman Professor of the Culture of Medicine at Harvard University, a member of the School's Department of Global Health and Social Medicine, and one of the co-organizers and curators of the exhibit.

His work as part of the team assembling the exhibit led him to appreciate the strength of the School's anatomical collections. "I've done a fair amount of teaching on the history of anatomy," says Jones, "and even I had no idea of the fascinating specimens the medical school has in storage."

—Stephanie Dutchen

CONNECT THE DOCS

THE COMMUNITY OF HARVARD MEDICAL SCHOOL ALUMNI



BEHIND THE SCENES: The creative team, and family, behind the film *American Promise* (from left): Joe Brewster, Idris Brewster, Miles Brewster, and Michèle Stephenson.

professor at McLean, he enrolled at The New School in New York with the aim of writing and producing films.

His first feature film, *The Keeper* (1996), a story of prison life, taught him the power of narrative.

"People were mesmerized by the way the prisoners and correctional officers spoke to one another, about their relationships, their vulnerabilities, and their similarities," he recalls.

Brewster says he's learned that being a successful psychiatrist and filmmaker depends on establishing trust with patients, actors, and audience.

"It's counterintuitive to share. It's like skiing: When you're going down a hill, you want to hold back to slow down, but great skiers lean forward," he says. "The therapeutic process involves teaching your patients to lean forward to control their lives."

"We had to learn to lean forward in *American Promise*," he adds. The documentary offers candid and, at times, unflattering depictions of Brewster, Stephenson, and their son. That level of honesty, however, proved transformative for the family, their community, and the school Idris attended. It was also powerful enough to earn the film the 2013 Special Jury Award for Achievement in Filmmaking from the Sundance Institute, which, in turn, led to its broadcast on PBS's *POV* series.

Almost 40 years after he applied to HMS, Brewster continues to stretch toward his goal of changing the world—from each patient he sees in his New York City practice to each "therapeutic community" he inspires with his films.

—Stephanie Dutchen

Framing the Issue

An HMS alumnus tackles social topics in his films and his practice

A YOUNG MAN LIES ON HIS BACK, an arm slung over his eyes, as he talks about what's bothering him. He's having trouble concentrating on homework. The basketball coach knocked him back to junior varsity. He's still not sure he fits in, as an African American teen, at the prestigious, historically white private school he attends in New York City.

Joe Brewster, Jr. '78, shot this scene involving his son Idris during the 13 years he was gathering material for the 2013 documentary *American Promise*, which Brewster directed and

produced. The film is one of eight works that Brewster and his wife Michèle Stephenson have completed for Rada Film Group, the production company they cofounded. Their films tackle topics ranging from post-traumatic stress (*The Killing Zone*) to racial issues in education (*American Promise*).

Brewster says his psychiatric training helps him develop complex characters whose willingness to share "difficult, uncomfortable stuff" brings them—and, Brewster hopes, audiences—to an epiphany that inspires change.

Since adolescence, Brewster has felt compelled to address social issues. A Los Angeles native, at age 12 he wrote Walt Disney, asking him to feature more African Americans in his movies. Later, at HMS, Brewster found a model for his media vision: Alvin Poussaint.

"Dr. Poussaint was on television and was featured in magazines and books in my home. Part of the way he made a difference was through the media," says Brewster. "It dawned on me that documentary filmmaking was one way I could reach people and, perhaps, change their lives."

Brewster financed his dream by fixing up old houses with friends while he was completing his residency at McLean Hospital. After a year as an HMS clinical

A POCKET GUIDE TO HMS ALUMNI

Alumni Association brings Doximity mobile app to its members

THE HARVARD MEDICAL ALUMNI ASSOCIATION (HMAA) has introduced a new mobile app powered by Doximity, a private virtual network for medical professionals. This app allows HMS graduates to reconnect, stay in touch, and interact with classmates and the HMAA network.

From the app's home page, alumni can access multiple features. The directory allows for searches by name, specialty, location, clinical interest, and within a range of graduation years. In addition to alumni contact information, profiles are intended to mirror professional CVs by highlighting training, research and publications, and clinical interests. There is also a private forum where alumni can discuss research and issues in medicine, solicit advice, exchange ideas, share experiences, and announce alumni news—all in real time. The app directly connects users to the home page for HMS alumni—hms.harvard.edu/alumni—where alumni may submit a class note to

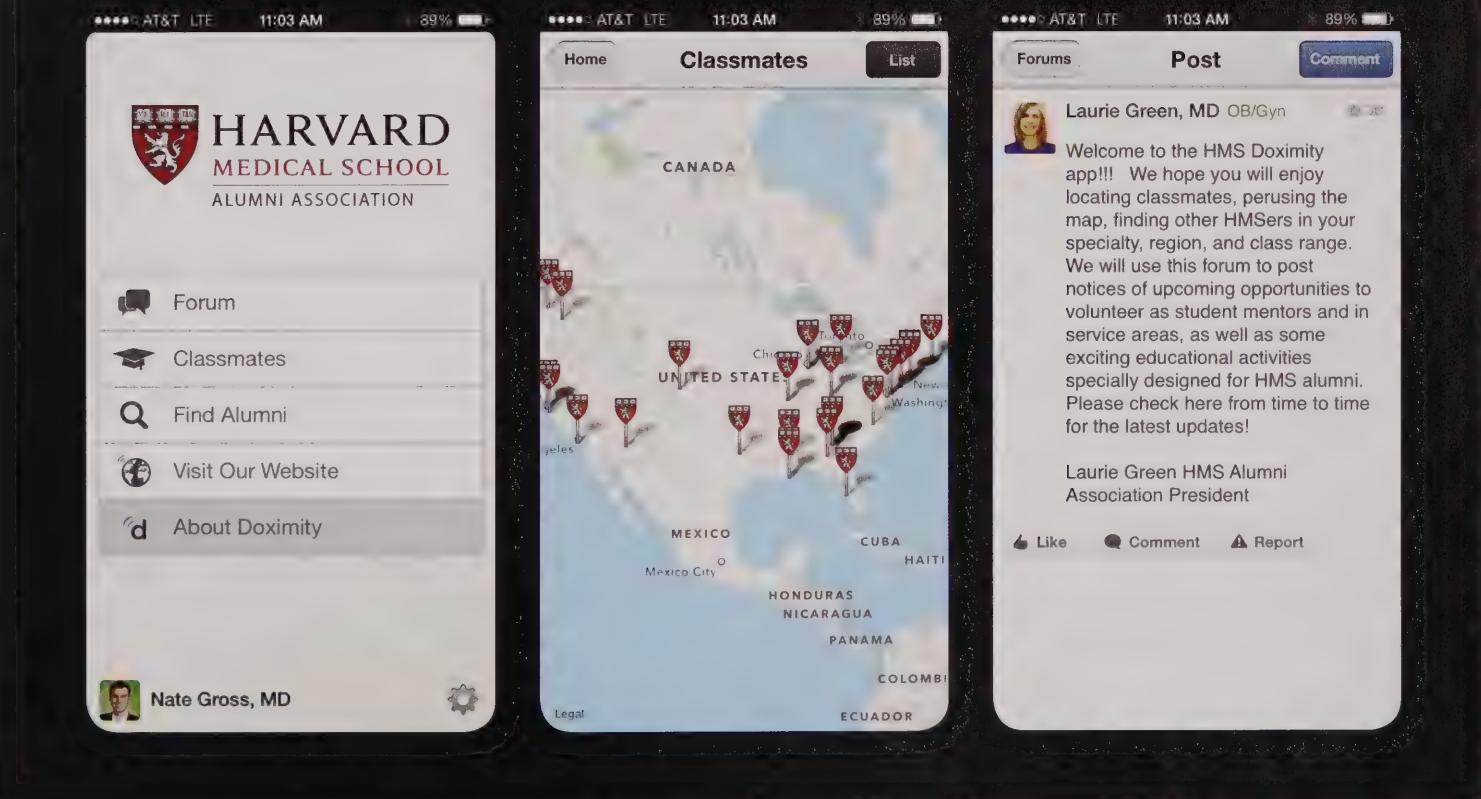
Harvard Medicine magazine, view the "In Memoriam" tribute section, find information about reunions and other events, explore opportunities for lifelong learning, and stay connected to HMS.

"The Alumni Council and HMAA are always looking for ways to keep alumni connected with each other and the School," says Laurie Green '76, president of the Alumni Council. "This tool provides HMS graduates with a secure, HIPAA-compliant alternative to traditional social networking sites."

The HMAA app was built in partnership with Doximity and can be downloaded for use on smartphones or computers. The Doximity network offers a suite of additional features for members, including a searchable directory of all U.S. physicians, HIPAA-compliant text messaging, free faxing from mobile phones and the web, and phone, fax, and office lines to hundreds of hospitals and facilities around the country. Users can customize their news digests to receive the latest news and journal articles on topics of their choice, while earning and tracking category 1 CME credits by reading articles.

To download the free app to your iPhone, iPod Touch, or iPad, search for "HMS Alumni" in the app store. Alumni who are already Doximity members should download the app to gain access to HMS-exclusive functions.

Since the app's launch in January, nearly 2,100 alumni have become members of the Harvard Medical School group.



CLASS NOTES

NEWS FROM ALUMNI

1945

Evan Calkins

After 38 years in academic medicine, I decided, at age 70, that it was time to practice medicine on my own. I set up a community-based private practice of rheumatology and geriatrics with two locations, in Buffalo and Hamburg, New York. It was wonderful! I retired at age 92, in order to be in the company of my wife, Virginia, and maintain closer contact with our 9 children, 30 grandchildren, and 4 great-grandchildren, many of whom join us for Christmas on the small farm where we have lived for the past 52 years.

Giulio D'Angio

I attended my 70th Columbia College class reunion last spring in New York with two other alumni. I also serve as our class agent. Shortly before that, my wife, Audrey, and I had been at the ordination of a pregnant priest—my granddaughter, the Rev. Sara D'Angio White. Her daughter, Margaret Rose ("Maggie"), was born in July. Deafness impedes my attending medical meetings, but I went to two. The first was the eighth International Conference on Pediatric Renal Tumor Biology, a series I started decades ago. Steady progress was reported by others smarter than me. The second was the inaugural lecture at Boston Children's Hospital of an annual oration I endowed in honor of Martin "Dick" and Harriett Wittenborg. Dick Wittenborg, a radiologist at that hospital, and his wife were important to me and many others as we matured in medicine.

Robert Post

Life in my retirement community is friendly, sociable, and interesting. I act in script-in-hand plays.

1947

Harold Braun

The California-Montana division of the Class of '47 had a mini-reunion in November at the Getty Museum in Los Angeles. Two members of our class, Henry Carleton and myself, were there and in good spirits.

Charles Hall

Some classmates are departing, and some are still kicking. I recently had an interesting visit to Morocco.

1949 **65th REUNION**

Francis Riley

After entering HMS 69 years ago, I'm still here at age 81, in fair health, and living alone in a retirement community, in Scottsdale, Arizona. I only wish that I had learned more about the aging process in medical school. Aging must have occurred even then, just earlier in life.

1956

John Grover

Three years in Chula Vista, California, have passed overnight! Philippa and I are well, making a lot of music and staying fit!

1958

John Livingstone

I am pleased to continue in the practice of psychotherapy, especially now that I have "modernized" myself in the latest advances with the prompting and partnership of my wife, Joanne, who is a continuing learner and advanced clinician. She and I have published



a book chapter on a new model of health coaching, which integrates health-related behavior change and medical decision making.

I was still skiing in the same old fast way until an accident two years ago, which signaled to me to stop trusting the feedback from my peripheral nerves. I continue working as a member of the HMS faculty. I took up rowing a single shell about 15 years ago after a long gap from my undergrad days at Brown University. My very best to all of my classmates who still walk this earth of ours.

1961

Robert Flescher

I still work one day a week in the GI Clinic at Hartford Hospital. I am currently recovering from knee replacement surgery, now in the stage of chronic aching, limited mobility, and diminished strength, but seeing steady, if slow, improvement.

Royce Moser, Jr.

Last November, I completed my terms as president-elect, president, and immediate past president of the Harvard School of Public Health Alumni Associa-

tion. I may never have graduated from HSPH (Class of 1965) had I not learned about aerospace medicine residency programs, which required a master of public health degree, while working one summer as a technician in a respiratory research project led by Charles "Dav" Cook '44 at Boston Children's Hospital. I have had two great careers, in the U.S. Air Force and at the University of Utah School of Medicine, and would not have been eligible for either without my HMS and HSPH degrees.

1962

Steven Jonas

I have retired as a professor in the Department of Preventive Medicine at the School of Medicine, Stony Brook, after serving more than 42 years. I remain on faculty as professor emeritus. I'm an elected Fellow of the New York Academy of Sciences, the American College of Preventive Medicine, the American Public Health Association, the New York Academy of Medicine, and the Royal Society of Medicine (UK).

Over the course of my career I have authored, co-authored, edited, and co-edited 34 books; more than 135 professional articles, book chapters, and book reviews; and delivered well over 100 papers at conferences and seminars.

1964 50th REUNION

Terry Bennett

I am a self-employed family doctor in a federally designated medically underserved community in Rochester, New Hampshire. I am now under treatment for an ampullary

(biliary tract) adenocarcinoma, which, unexpectedly, expresses a breast cancer protein, HER2. I was able to get access to Kadlecra, a new breast cancer drug, which has kept me going for two years. I plan to attend our 50th reunion, assuming I am still vertical.

James Sabin

One of my post-practice activities is contributing to Over 65, a blog on aging published by The Hastings Center.

George Sarosi

I am attending eight months a year on the wards of the Minneapolis VA with residents and students from the University of Minnesota Medical School.

Douglas Zipes

I published my second novel, a medical thriller, *Ripples in Opperman's Pond*.

1966

Dennis Bauman

I am still practicing part time in Elkin, North Carolina. The practice is challenging, with 75 percent of patients on Medicaid, but medicine remains rewarding. We appreciate the climate, beauty, and affordable golf in North Carolina.

1967

William Saxbe, Jr.

In October, I was elected president of the American Society of Genealogists, a scholarly group limited to 50 living Fellows. Elections are based on the quality and quantity of publications. I have been a certified genealogist since 1981, and was elected to the Society in 1997.

1968

Stephanie Pincus

My oldest child married his long-time partner in New York City in November. My daughter has a thriving sex therapy practice in Washington, DC, and my youngest son has started a PhD program in health policy at Harvard. I will be moving to Manhattan in 2014, and look forward to seeing classmates in the Big Apple.

John Welch

I retired in December 2012, after working at Hartford Hospital in Connecticut for 34 years. I am thoroughly enjoying this different lifestyle.



CLASS NOTES

NEWS FROM ALUMNI

1969 **45th**
REUNION

Elizabeth Thomas Anderson Mayer

I have been retired for five years. I enjoy my life and surprisingly don't miss medicine as I thought I would. I'm a volunteer teacher at the Joint Medical Program of UC Berkeley and UC San Francisco, the Friday babysitter for my granddaughter Dorothea, and was a recent visitor to St. John where I celebrated my 70th birthday with the whole family.

1970

Kenneth Berv

I continue to work in a solo psychiatric practice, attend performances at Carnegie Hall and the Metropolitan Opera, play horn, swim five times a week, and dance salsa. It is my son's last year at the Jacobs School of Music in Indiana. And my biologist/tropical ornithologist son is in his first year of graduate school at Cornell.

thologist son is in his first year of graduate school at Cornell.

1972

Kim Masters

I am the medical director and child and adolescent psychiatrist at the 62-bed Three Rivers Midlands Campus Residential Treatment Center in West Columbia, South Carolina. As part of my work, I teach three to four physician assistant students each month on their clinical psychiatry rotations from the Medical University of South Carolina and the Wake Forest School of Medicine.

1973

David Lee

I still believe in primary care and am still practicing in Boise, Idaho, a wondrous community.

1974 **40th**
REUNION

Edmond Raker

I still enjoy practicing vascular surgery and training residents at Virginia Mason Hospital and Medical Center in Seattle. Marie and I are grandparents—times two! All three sons married excellent women and are doing well.

William Watters III

I continue in active practice as an orthopedic spinal surgeon at the Texas Medical Center in Houston, and, in October, began my presidential year at the North American Spine Society.

1976

David Nierenberg

My wife, Joan, is retired now, but I'm still working full time. I'm also enjoying teaching, course direction, and clinical consulting. I am more involved now in the local free clinic, playing cello in local ensembles, and visiting our first grandchild! Please visit when you pass through New Hampshire.

1979 **35th**
REUNION

Richard Rowe

I'm still running—and getting nowhere. I finished the Ironman Lake Tahoe in September, fortunately the day before hard 50-mph winds and snow arrived in the area. I will be back in Boston to run the marathon again!

1985

Sheryl Spitzer-Resnick

I am now specializing in women's

health and integrative medicine in Madison, Wisconsin.

1999 **15th**
REUNION

Lena Kim

I am a maternal-fetal medicine faculty member at UC San Francisco and live in Marin County with my husband and two children.

Nerissa Koehn

I recently moved back home to Missoula, Montana, to become the associate program director of the newly established Family Medicine Residency of Western Montana. My husband, John Miller, and I celebrated the birth of our third daughter, Olympia Gabriella Koehn Miller, on September 17, 2013. Olympia joins sisters Sophia and Alexandria.

2004 **10th**
REUNION

Sallie Permar

I have been selected to receive the Presidential Early Career Award for Scientists and Engineers, an award presented by the U.S. government to science and engineering professionals in the early stages of their independent research careers.

Share Your News

If you have updates you'd like to share in Class Notes, you can now submit them easily and securely to class-notes@hms.harvard.edu. Be sure to include your full name and class year.



OBITUARIES

REMEMBERING DISTINGUISHED LIVES

1930s

1938

Hunt B. Jones
February 14, 2014

1939

William Altman
January 27, 2014

1940s

1942

Philip K. Bondy
October 14, 2013

William R. Christensen
December 14, 2014

Cully A. Cobb, Jr.
November 23, 2013

1943

Robert D. Ray
October 12, 2013

1944

Wiley F. Barker
October 31, 2013

Lewis A. Barness
November 18, 2013

1946

Milton W. Hamolsky
January 18, 2014

Theodore H. Wilson, Jr.
December 16, 2013

1947

John S. Avery
October 23, 2013

Norman J. Silverstone
November 5, 2013

1948

David L. Chamovitz
January 6, 2014

John F. Hogan
October 26, 2013

Elwood F. Ireland, Jr.
February 9, 2014

1949

Marsden E. Fox
October 17, 2013

Edward J. Leonard
December 25, 2013

Victor A. Marcial
December 7, 2013

1950s

1950

Alan C. Aisenberg
October 27, 2013

Lloyd W. Merryfield
December 7, 2013

1951

Francis L. Sult
December 20, 2013

1952

Frank A. Costanzo
October 31, 2013

James A. Pittman, Jr.
January 12, 2014

1953

George Eisenman
December 11, 2013

Warren L. Franz
December 19, 2013

1948

Stuart H. Mudd

January 21, 2014

1954

Monto Ho
December 16, 2013

N. Conant Webb, Jr.
September 11, 2013

1949

Bernard Kliman
January 30, 2014

1955

Joel J. Alpert
December 31, 2013

William E. Hitselberger
February 13, 2014

Henry L. Laws II
February 25, 2014

1957

Peter R. Huttenlocher
May 15, 2013

1959

Bucknam McPeek
December 26, 2013

Harold W. Williams, Jr.
August 28, 2013

1960s

1960

Richard K. Myler
October 9, 2013

1962

Robert C. Moellering, Jr.
February 24, 2014

1963

Robert E. Rawitscher
October 16, 2013

1965

Alan S. King
October 14, 2013

1967

Arthur S. Schantz
January 15, 2014

1969

John Noseworthy
November 5, 2013

1970s

1972

Andrew K. Diehl
December 24, 2013

Stephen J. Lipson
December 17, 2013

1974

Sergei Bogojavlensky
October 19, 2013

This listing of deceased alumni and their dates of death include those alumni whose notices of death were received between October 18, 2013, and March 7, 2014. Links to full obituaries of these alumni can be found at hms.harvard.edu/memoriam.

If you know of an HMS alumna/us who has died recently, please send an email with the link to the obituary to hmsalum@hms.harvard.edu.

TAKING A HISTORY

PROFILE OF MARK ADICKES



CLAIMS TO FAME Assistant professor, Department of Orthopedic Surgery, University of Texas Medical School; professional football player, Kansas City Chiefs and Washington Redskins; commentator, ESPN.

FIRST DOWN A love of football was rooted in Mark Adickes' upbringing. Football was such a defining presence that throughout his childhood, Adickes '00 dreamed of becoming a football coach. His aptitude for playing the sport led him to earn a scholarship to Baylor

University, where he was named an NCAA All-American.

In 1986, after two seasons with the U.S. Football League, Adickes was drafted by the National Football League in the first round, and played for the Kansas City Chiefs through the 1989 season, then for the Washington Redskins in 1990, and in 1991, when he helped Washington win the Super Bowl.

"The experience of being part of a team, the camaraderie of a pretty amazing group of guys, and winning the Super Bowl and receiving a Super Bowl ring; all those memories are icing on the cake," says Adickes.

After retiring from the NFL, he concentrated on combining his career as a professional athlete with his interests in health care, physical therapy, and medicine.

TWO-POINT CONVERSION

Adickes attended George Mason University in Virginia to fulfill his medical school requirements, but hadn't planned on applying to HMS until his wife encouraged him to. At the end of his education at HMS, Adickes was once again tapped for a pinnacle event: He was selected as a student commencement speaker.

A residency in orthopedic surgery at the Mayo Clinic in Rochester, Minnesota, was followed by a sports medicine fellowship at the Steadman Hawkins Clinic in Vail, Colorado. "I love being in the OR," he says.

Adickes is now an orthopedic surgeon at the University of Texas Medical School in Houston and co-medical director of the Ironman Sports Medicine Institute at Memorial Hermann Hospital.

THEATER TO SCREEN A typical day for Adickes begins at 5:00 a.m., often with his first

Adickes was drafted by the NFL in the first round, and played for the Kansas City Chiefs through the 1989 season, then for the Washington Redskins in 1990 and in 1991.

surgery of the day starting at 6:00 a.m. Each week, he performs about 15 surgeries, which are often arthroscopic treatments of knee, shoulder, and hip injuries. In clinic, he sees up to 60 patients daily, many of them elite athletes.

Adickes notes that working with professional athletes requires coordinating communication between an athlete's manager, agent, and coach, and discussing such issues as whether the athlete is physically and mentally ready to return to the sport.

"You're under the microscope when you're taking care of elite athletes," he says.

In late 2013, he kicked off his latest venture: sports medicine expert for ESPN. From his home studio, he gets looped into conversations about athletes' injuries and prognoses. He also was the host of *Athlete 360*, a sports medicine television show on Fox Sports Net.

When he's not seeing patients or serving as a TV doc, Adickes can usually be found at one of his five kids' sporting or arts events.

"My spare time totally revolves around family. My kids are involved with sports, arts, drama, so I go to all those events."

—Katie DuBoff



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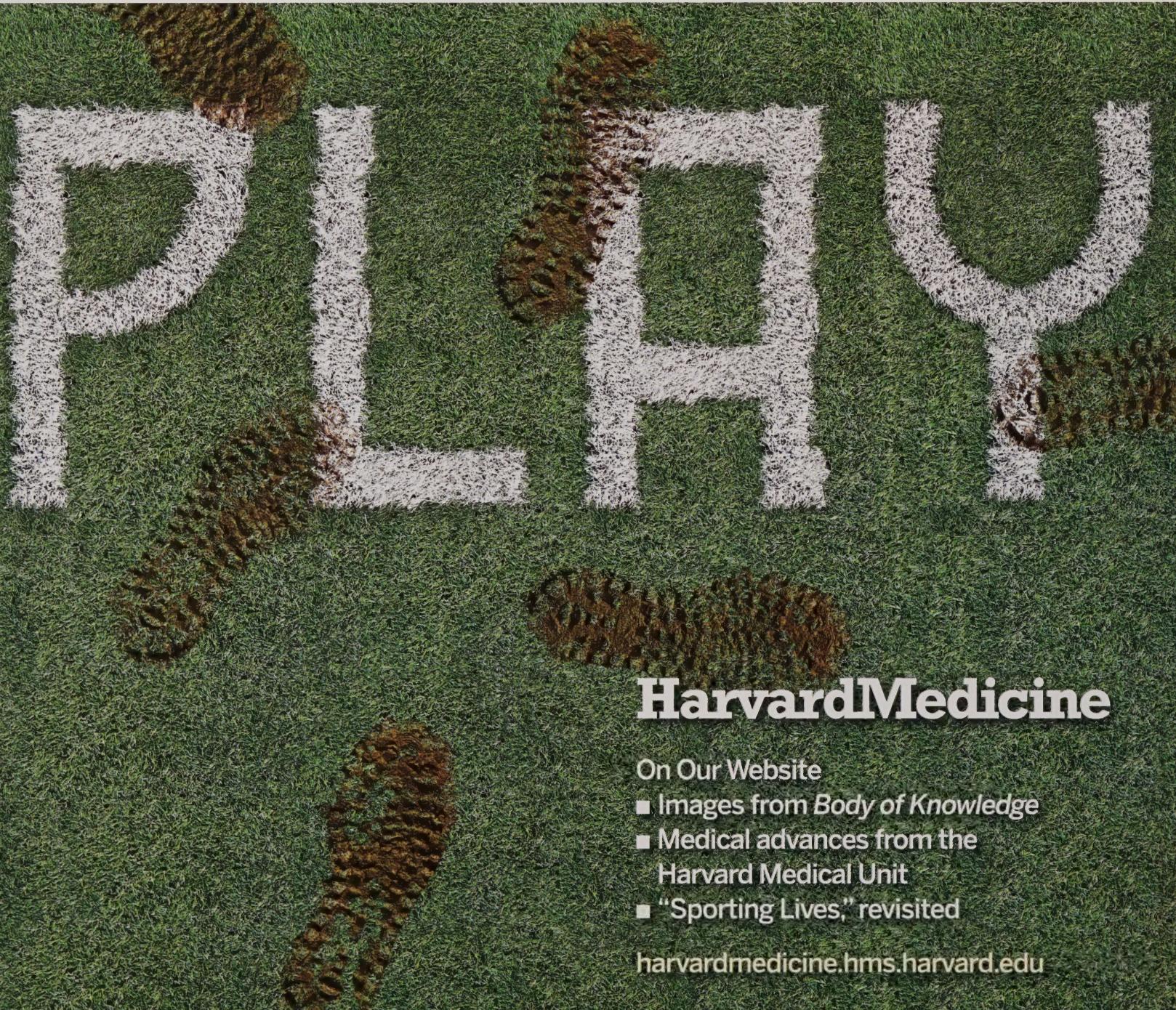
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